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12AP1/F5 -- Viventia Biotech 1964 -- Aventis 20K growth hormone -- AMUR 28P6/E6 -- Viventia Biotech 3-Hydroxyphthaloyl-beta-lactoglobulin -4-IBB ligand gene therapy -64-Cu MAb conjugate TETA-1A3 --Mallinckrodt Institute of Radiology 64-Cu MAb conjugate TETA-cT84.66 64-Cu Trastuzumab TETA conjugate -Genentech A 200 -- Amgen A10255 - Eli Liliv A1PDX - Hedral THerapeutics A6 -- Anastrom aaAT-III -- Genzvme Abciximab -- Centocor ABI.001 - Atlantic BioPharmaceuticals ABT-828 - Abbott Accutin Actinohivin activin -- Biotech Australia, Human Therapeutics activin -- Curls AD 439 - Tanox AD 519 - Tanox Adalimumab -- Cambridge Antibody Tech. Adenocarcinoma vaccine - Biomira - NIS Adenosine A2B receptor antagonists --Adenosine Therapeutics ADP-001 - Axis Genetics AF 13948 - Affymax Afelimomab – Knoll AFP-SCAN - Immunomedics AG 2195 - Corixa agalsidase alfa -- Transkaryotic Therapies agalsidase beta -- Genzyme AGENT-Antisoma AI 300 - AutoImmune AI-101 - Teva

Al-102 - Teva

Al-201 - AutoImmune Al-301 - Autolmmune AIDS vaccine - ANRS, CIBG, Hesed Biomed, Hollis-Eden, Rome, United Biomedical, American Home Products, Maxvgen airway receptor ligand -- IC Innovations - AJvW 2 -- Ajinomoto AK 30 NGF -- Alkermes Albuferon - Human Genome Sciences albumin - Biogen, DSM Anti-Infectives, Genzyme Transgenics, PPL Therapeutics, TranXenoGen, Welfide Corp. aldesleukin - Chiron alefacept -- Biogen Alemtuzumab -Allergy therapy -- ALK-Abello/Maxygen, Al K-Abello/RP Scherer allergy vaccines -- Allergy Therapeutics Alnidofibatide -- Aventis Pasteur Alnorine -- SRC VB VECTOR ALP 242 -- Gruenenthal Alpha antitrypsin -- Arriva/Hyland Immuno/ProMetic/Protease Sciences Alpha-1 antitrypsin - Cutter, Bayer, PPL Therapeutics, Profile, ZymoGenetics, Arriva Alpha-1 protease inhibitor -- Genzyme Transgenics, Welfide Corp. Alpha-galactose fusion protein -**Immunomedics** Alpha-galactosidase A -- Research Corporation Technologies Alpha-glucosidase - Genzyme, Novazyme Alpha-lactalbumin Alpha-L-iduronidase - Transkaryotic Therapies, BioMarin alteplase -- Genentech alvircept sudotox -- NIH ALX1-11 -sNPS Pharmaceuticals Alzheimer's disease gene therapy -

FIG. 1A

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Anti-B4 MAb-DC1 conjugate - ImmunoGen AM-133 -- AMRAD Anti-B7 antibody PRIMATIZED -- IDEC Amb a 1 immunostim conj. - Dynavax Anti-B7-1 MAb 16-10A1 AMD 3100 - AnorMED -- NIS Anti-B7-1 MAb 1G10 AMD 3465 - AnorMED -- NIS Anti-B7-2 MAb GL-1 AMD 3465 - AnorMED -- NIS Anti-B7-2-gelonin immunotoxin -AMD Fab -- Genentech Antibacterials/antifungals --Amediplase - Menarini, Novartis Diversa/IntraBiotics AM-F9 Anti-beta-amyloid monoclonal antibodies --Amoebiasis vaccine Cambridge Antibody Tech., Wyeth-Averst Amphiregulin -- Octagene Anti-BLvS antibodies -- Cambridge anakinra - Amgen Antibody Tech. /Human Genome Sciences analgesic -- Nobex Antibody-drug conjugates - Seattle ancestim -- Amgen Genetics/Eos AnergiX.RA - Corixa, Organon Anti-C5 MAb BB5-1 -- Alexion Angiocidin - InKine Anti-C5 MAb N19-8 -- Alexion angiogenesis inhibitors -- ILEX Anti-C8 MAb AngioMab - Antisoma anticancer cytokines - BioPulse Angiopoietins -- Regeneron/Procter & anticancer matrix - Telios Integra Gamble Anticancer monoclonal antibodies - ARIUS, angiostatin -- EntreMed Angiostatin/endostatin gene therapy -Immunex anticancer peptides - Maxygen, Micrologix Genetix Pharmaceuticals Anticancer prodrug Tech. -- Alexion angiotensin-II, topical -- Maret Anthrax -- EluSvs Therapeutics/US Army Antibody Technologies anticancer Troy-Bodies -- Affite -- Affitech Medical Research Institute anticancer vaccine -- NIH Anthrax vaccine Anti platelet-derived growth factor D human anticancers - Epimmune Anti-CCR5/CXCR4 sheep MAb -- KS monoclonal antibodies -- CuraGen Biomedix Holdings Anti-17-1A MAb 3622W94 --Anti-CD11a MAb KBA -GlaxoSmithKline Anti-CD11a MAb M17 Anti-2C4 MAb -- Genentech anti-4-1BB monoclonal antibodies -- Bristol- Anti-CD11a MAb TA-3:-Anti-CD11a MAb WT.1 -Myers Squibb Anti-CD11b MAb -- Pharmacia Anti-Adhesion Platform Tech. -- Cytovax Anti-adipocyte MAb -- Cambridge Antibody Anti-CD11b MAb LM2 Anti-CD154 MAb - Biogen Tech./ObeSys Anti-CD16-anti-CD30 MAb - Biotest antiallergics -- Maxygen Anti-CD18 MAb -- Pharmacia antiallergy vaccine - Acambis Anti-CD19 MAb B43 -Anti-alpha-4-integrin MAb Anti-angiogenesis monocional antibodies -- Anti-CD19 MAb -liposomal sodium butyrate conjugate -KS Biomedix/Schering AG

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Anti-CD4 MAb GK1-5

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Anti-CD4 MAb KT6 Anti-CD19 MAb-saporin conjugate -Anti-CD19-dsFv-PE38-immunotoxin -Anti-CD4 MAb OX38 Anti-CD4 MAb PAP conjugate -- Bristol-Anti-CD2 MAb 12-15 -Myers Squibb Anti-CD2 MAb B-E2 -- Diaclone Anti-CD4 MAb RIB 5-2 Anti-CD2 MAb OX34 --Anti-CD4 MAb W3/25 Anti-CD2 MAb OX54 -Anti-CD4 MAb YTA 3.1.2 Anti-CD2 MAb OX55 -Anti-CD4 MAb YTS 177-9 Anti-CD2 MAb RM2-1 Anti-CD40 ligand MAb 5c8 -- Biogen Anti-CD2 MAb RM2-2 Anti-CD40 MAb Anti-CD2 MAb RM2-4 Anti-CD40 MAb 5D12 - Tanox Anti-CD20 MAb BCA B20 Anti-CD20-anti-Fc alpha RI bispecific MAb -Anti-CD44 MAb A3D8 Anti-CD44 MAb GKWA3 Medarex, Tenovus Anti-CD44 MAb IM7 Anti-CD22 MAb-saporin-6 complex -Anti-CD44 MAb KM81 Anti-CD3 immunotoxin -Anti-CD44 variant monoclonal antibodies --Anti-CD3 MAb 145-2C11 -- Pharming Corixa/Hebrew University Anti-CD3 MAb CD4lgG conjugate --Anti-CD45 MAb BC8-I-131 Genentech Anti-CD3 MAb humanised - Protein Design, Anti-CD45RB MAb Anti-CD48 MAb HuLv-m3 RW Johnson Anti-CD48 MAb WM-63 Anti-CD3 MAb WT32 Anti-CD5 MAb -- Becton Dickinson Anti-CD3 MAb-ricin-chain-A conjugate -Anti-CD3 MAb-xanthine-oxidase conjugate Anti-CD5 MAb OX19 Anti-CD6 MAb Anti-CD7 MAb-PAP conjugate Anti-CD30 MAb BerH2 -- Medac Anti-CD7 MAb-ricin-chain-A conjugate Anti-CD30 MAb-saporin conjugate Anti-CD8 MAb - Amerimmune, Cytodyn, Anti-CD30-scFv-ETA'-immunotoxin Becton Dickinson Anti-CD38 MAb AT13/5 Anti-CD8 MAb 2-43 Anti-CD38 MAb-saporin conjugate Anti-CD8 MAb OX8 Anti-CD3-anti-CD19 bispecific MAb Anti-CD80 MAb P16C10 -- IDEC Anti-CD3-anti-EGFR MAb Anti-CD80 MAb P7C10 - ID Vaccine Anti-CD3-anti-interleukin-2-receptor MAb Anti-CD8-idarubicin conjugate Anti-CD3-anti-MOv18 MAb -- Centocor Anti-CEA MAb CE-25 Anti-CD3-anti-SCLC bispecific MAb Anti-CEA MAb MN 14 - Immunomedics Anti-CD4 idiotype vaccine Anti-CEA MAb MN14-PE40 conjugate -Anti-CD4 MAb - Centocor, IDEC **Immunomedics** Pharmaceuticals, Xenova Group Anti-CEA MAb T84.66-interleukin-2 Anti-CD4 MAb 16H5 Anti-CD4 MAb 4162W94 -- GlaxoSmithKline conjugate Anti-CEA sheep MAb -- KS Biomedix Anti-CD4 MAb B-F5 -- Diaclone

Holdings

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Anti-HIV antibody - Epicyte Anti-cell surface monoclonal antibodies -anti-HIV catalytic antibody - Hesed Biomed Cambridge Antibody Tech. /Pharmacia Anti-c-erbB2-anti-CD3 bifunctional MAb anti-HIV fusion protein - Idun anti-HIV proteins -- Cangene Otsuka Anti-HM1-24 MAb -- Chugai Anti-CMV MAb - Scotgen Anti-hR3 MAb Anti-CTLA-4 MAb Anti-Human-Carcinoma-Antigen MAb --Anti-EGFR catalytic antibody -- Hesed Epicyte Biomed Anti-ICAM-1 MAb -- Boehringer Ingelheim anti-FGFR immunotoxin -- IVAX Anti-ICAM-1 MAb 1A-29 -- Pharmacia Anti-EGFR MAb -- Abgenix Anti-ICAM-1 MAb HA58 Anti-EGFR MAb 528 Anti-ICAM-1 MAb YN1/1.7.4 Anti-EGFR MAb KSB 107 - KS Biomedix Anti-ICAM-3 MAb ICM3 -- ICOS Anti-EGFR MAb-DM1 conjugate --Anti-idiotype breast cancer vaccine 11D10 ImmunoGen Anti-idiotype breast cancer vaccine Anti-EGFR MAb-LA1 -ACA14C5 -Anti-EGFR sheep MAb -- KS Biomedix Anti-idiotype cancer vaccine -- ImClone Anti-FAP MAb F19-I-131 Systems/Merck KGaA ImClone, Viventia Anti-Fas IgM MAb CH11 Biotech Anti-Fas MAb Jo2 Anti-idiotype cancer vaccine 1A7 -- Titan Anti-Fas MAb RK-8 Anti-Flt-1 monoclonal antibodies - ImClone Anti-idiotype cancer vaccine 3H1 - Titan Anti-idiotype cancer vaccine TriAb -- Titan Anti-fungal peptides -- State University of Anti-idiotype Chlamydia trachomatis New York vaccine antifungal tripeptides -- BTG Anti-ganglioside GD2 antibody-interleukin-2 Anti-idiotype colorectal cancer vaccine --Novartis fusion protein -- Lexigen Anti-idiotype colorectal cancer vaccine --Anti-GM2 MAb -- Kyowa Anti-GM-CSF receptor monoclonal Onvvax Anti-idiotype melanoma vaccine - IDEC antibodies -- AMRAD Anti-gp130 MAb -- Tosoh Pharmaceuticals 3 3 2 Anti-idiotype ovarian cancer vaccine ACA Anti-HCA monoclonal antibodies --AltaRex/Epigen Anti-idiotype ovarian cancer vaccine AR54 -Anti-hCG antibodies -- Abgenix/AVI AltaRex BioPharma Anti-idiotype ovarian cancer vaccine CA-Anti-heparanase human monoclonal 125 – AltaRex. Biomira antibodies -- Oxford Anti-IgE catalytic antibody -- Hesed Biomed Glycosciences/Medarex Anti-IgE MAb E26 -- Genentech Anti-hepatitis C virus human monoclonal antibodies -- XTL Biopharmaceuticals Anti-IGF-1 MAb anti-inflammatory - GeneMax Anti-HER-2 antibody gene therapy anti-inflammatory peptide -- BTG Anti-herpes antibody -- Epicyte

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Anti-mu MAb -- Novartis anti-integrin peptides -- Burnha Anti-interferon-alpha-receptor MAb 64G12 -- Anti-MUC-1 MAb Anti-Nogo-A MAb IN1 Pharma Pacific Management Anti-nuclear autoantibodies - Procyon Anti-interferon-gamma MAb -- Protein Anti-ovarian cancer monoclonal antibodies -Design Labs Anti-interferon-gamma polyclonal antibody - - Dompe Anti-p185 monoclonal antibodies - Advanced Biotherapy Anti-p43 MAb Anti-interleukin-10 MAb -Antiparasitic vaccines Anti-interleukin-12 MAb -Anti-interleukin-1-beta polyclonal antibody -- Anti-PDGF/bFGF sheep MAb -- KS Biomedix R&D Systems Anti-properdin monoclonal antibodies ---Anti-interleukin-2 receptor MAb 2A3 Abgenix/Gliatech Anti-interleukin-2 receptor MAb 33B3-1 --Anti-PSMA MAb J591 -- BZL Biologics Immunotech Anti-Rev MAb gene therapy -Anti-interleukin-2 receptor MAb ART-18 Anti-RSV antibodies - Epicyte, Intracell Anti-interleukin-2 receptor MAb LO-Tact-1 Anti-RSV monoclonal antibodies --Anti-interleukin-2 receptor MAb Mikbeta1 Medarex/Medimmune, Applied Molecular Anti-interleukin-2 receptor MAb NDS61 Evolution/MedImmune Anti-interleukin-4 MAb 11B11 Anti-RSV MAb, inhalation -Anti-interleukin-5 MAb -- Wallace Alkermes/Medimmune Laboratories Anti-RT gene therapy Anti-interleukin-6 MAb - Centocor, Antisense K-ras RNA gene therapy Diaclone, Pharmadigm Anti-SF-25 MAb Anti-interleukin-8 MAb - Xenotech Anti-sperm antibody -- Epicyte Anti-.II 1 MAb Anti-Tac(Fv)-PE38 conjugate Anti-Klebsiella sheep MAb -- KS Biomedix Anti-TAPA/CD81 MAb AMP1 Holdings Anti-tat gene therapy Anti-Laminin receptor MAb-liposomal Anti-TCR-alphabeta MAb H57-597 doxorubicin conjugate Anti-TCR-alphabeta MAb R73 Anti-LCG MAb -- Cytoclonal Anti-tenascin MAb BC-4-1-131 Anti-lipopolysaccharide MAb -- VitaResc Anti-TGF-beta human monoclonal Anti-L-selectin monoclonal antibodies -antibodies - Cambridge Antibody Tech., Protein Design Labs, Abgenix, Stanford Genzyme University Anti-TGF-beta MAb 2G7 -- Genentech Anti-MBL monoclonal antibodies --Antithrombin III -- Genzyme Transgenics, Alexion/Brigham and Women's Hospital Aventis, Bayer, Behringwerke, CSL, Anti-MHC monoclonal antibodies Anti-MIF antibody humanised - IDEC, Myriad Anti-Thy1 MAb Cytokine PharmaSciences Anti-Thy1.1 MAb Anti-MRSA/VRSA sheep MAb -- KS Biomedix Holdings

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Anti-tissue factor/factor VIIA sheep MAb -- ARGENT gene delivery systems -- ARIAD KS Biomedix Arresten Anti-TNF monoclonal antibodies -ART-123 -- Asahi Kasei arylsulfatase B -- BioMarin Centocor, Chiron, Peptech, Pharacia, Arylsulfatase B, Recombinant human --Serono Anti-TNF sheep MAb - KS Biomedix BioMarin AS 1051 -- Aiinomoto Holdings ASI-BCL -- Intracell Anti-TNFalpha MAb - Genzyme Anti-TNFalpha MAb B-C7 -- Diaclone ATL-101 - Alizyme atrial natriuretic peptide - Pharis Anti-tooth decay MAb -- Planet BioTech. Aurintricarboxylic acid-high molecular antitumour RNases -- NIH Anti-VCAM MAb 2A2 -- Alexion weight autoimmune disorders -- GPC Anti-VCAM MAb 3F4 -- Alexion Biotech/MorphoSys Anti-VCAM-1 MAb Autoimmune disorders and transplant Anti-VEC MAb -- ImClone rejection -- Bristol-Myers Squibb/Genzyme Anti-VEGF MAb -- Genentech Anti-VEGF MAb 2C3 Tra Autoimmune disorders/cancer --Anti-VEGF sheep MAb -- KS Biomedix Abgenix/Chiron, /CuraGen Holdings Autotaxin Anti-VLA-4 MAb HP1/2 -- Biogen Avicidin -- NeoRx Anti-VLA-4 MAb PS/2 axogenesis factor-1 - Boston Life Sciences Anti-VLA-4 MAb R1-2 Axokine -- Regeneron Anti-VLA-4 MAb TA-2 Anti-VRE sheep MAb -- KS Biomedix B cell lymphoma vaccine -- Biomira B7-1 gene therapy -Holdings BABS proteins -- Chiron ANUP -- TranXenoGen BAM-002 - Novelos Therapeutics ANUP-1 -- Pharis AOP-RANTES -- Senetek Bav-16-9996 -- Bayer Apan-CH -- Praecis Pharmaceuticals Bay-39-9437 -- Bayer Bay-50-4798 -- Bayer APC-8024 -- Demegen ApoA-1 -- Milano, Pharmacia BB-10153 -- British Biotech BBT-001 - Bolder BioTech. Apogen -- Alexion BBT-002 -- Bolder BioTech. apolipoprotein A1 -- Avanir BBT-003 -- Bolder BioTech. Apolipoprotein E -- Bio-Tech. General BBT-004 -- Bolder BioTech. Applaggin -- Biogen BBT-005 -- Bolder BioTech. aprotinin -- ProdiGene BBT-006 -- Bolder BioTech. APT-070C -- AdProTech BBT-007 -- Bolder BioTech. AR 177 -- Aronex Pharmaceuticals AR 209 -- Aronex Pharmaceuticals, BCH-2763 -- Shire BCSF - Millenium Biologix Antigenics BDNF - Regeneron - Amgen AR545C

FIG. 1F

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Becaplermin - Johnson & Johnson, Chiron BST-3002 - BioStratum Bectumomab - Immunomedics BTI 322 butvrvicholinesterase -- Shire Beta-adrenergic receptor gene therapy --C 6822 -- COR Therapeutics University of Arkansas Bi 51013 -- Behringwerke AG C1 esterase inhibitor -- Pharming C3d adiuvant -- AdProTech BIBH 1 - Boehringer Ingelheim CAB-2.1 -- Millennium BIM-23190 -- Beaufour-lpsen calcitonin - Inhale Therapeutics Systems, birch pollen immunotherapy -- Pharmacia bispecific fusion proteins -- N1H Aventis, Genetronics, TranXenoGen, Unigene, Rhone Poulenc Rohrer Bispecific MAb 2B1 -- Chiron Bitistatin calcitonin - oral - Nobex, Emisphere, BIWA 4 - Boehringer Ingelheim Pharmaceutical Discovery Calcitonin gene-related peptide -- Asahi blood substitute - Northfield, Baxter Intl. Kasei -- Unigene BLP-25 -- Biomira BLS-0597 -- Boston Life Sciences calcitonin, human -- Suntory BLvS -- Human Genome Sciences calcitonin, nasal - Novartis, Unigene BLvS radiolabelled -- Human Genome calcitonin, Panoderm -- Elan Sciences calcitonin, Peptitrol -- Shire calcitonin, salmon -- Therapicon BM 06021 --- Boehringer Mannheim BM-202 -- BioMarin calin -- Biopharm Calphobindin I BM-301 -- BioMarin BM-301 -- BioMarin calphobindin I -- Kowa calreticulin -- NYU BM-302 -- BioMarin BMP 2 - Genetics Institute/Medtronic-Campath-1G Sofamor Danek, Genetics Institute/ Campath-1M Collagenesis, Genetics cancer therapy -- Cangene cancer vaccine - Aixlie, Aventis Pasteur, Institute/Yamanouch Center of Molecular Immunology, YM BMP 2 gene therapy BMP 52 - Aventis Pasteur, Biopharm BioSciences, Cytos, Genzyme, BMP-2 -- Genetics Institute Transgenics, Globelmmune, Igeneon, BMS 182248 -- Bristol-Myers Squibb ImClone, Virogenetics, InterCell, Iomai, BMS 202448 -- Bristol-Myers Squibb Jenner Biotherapies, Memorial Sloan-Kettering Cancer Center, Sydney Kimmel bone growth factors -- IsoTis BPC-15 -- Pfizer Cancer Center, Novavax, Protein Sciences, Argonex, SIGA brain natriuretic peptide -Cancer vaccine ALVAC-CEA B7.1 --Breast cancer -- Oxford GlycoSciences/Medarex Avents Pasteur/Therion Biologics Breast cancer vaccine -- Therion Biologics, Cancer vaccine CEA-TRICOM -- Aventis Pasteur/Therion Biologics Oregon BSSL -- PPL Therapeutics Cancer vaccine gene therapy -- Cantab BST-2001 - BioStratum Pharmaceuticals 2 4 1

FIG. 1G

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Cancer vaccine HER-2/neu -- Corixa CETP vaccine -- Avant Cancer vaccine THERATOPE -- Biomira Cetrorelix cancer vaccine, PolyMASC -- Valentis Cetuximab Candida vaccine - Corixa, Inhibitex CGH 400 -- Novartis CGP 42934 - Novartis Canstatin -- ILEX CGP 51901 - Tanox CAP-18 -- Panorama Cardiovascular gene therapy -- Collateral CGRP -- Unigene CGS 27913 -- Novartis Therapeutics CGS 32359 -- Novartis carperitide -- Suntory Chagas disease vaccine -- Corixa Casocidin-1 -- Pharis CAT 152 -- Cambridge Antibody Tech. chemokines -- Immune Response CHH 380 -- Novartis CAT 192 -- Cambridge Antibody Tech. chitinase - Genzyme, ICOS CAT 213 - Cambridge Antibody Tech. Chlamydia pneumoniae vaccine -- Antex Catalase -- Enzon Biologics Cat-PAD -- Circassia Chlamydia trachomatis vaccine -- Antex CB 0006 -- Celltech **Biologics** CCK(27-32)-- Akzo Nobel Chlamydia vaccine - GlaxoSmithKline CCR2-641 -- NIH Cholera vaccine CVD 103-HgR -- Swiss CD, Procept -- Paligent Serum and Vaccine Institute Berne CD154 gene therapy Cholera vaccine CVD 112 -- Swiss Serum CD39 -- Immunex and Vaccine Institute Berne CD39-L2 -- Hvseq Cholera vaccine inactivated oral -- SBL CD39-L4 -- Hvsea CD4 fusion toxin - Senetek Vaccin Chrysalin - Chrysalis BioTech. CD4 lgG -- Genentech CI-782 -- Hitachi Kase CD4 receptor antagonists ---Ciliary neurotrophic factor - Fidia, Roche Pharmacopeia/Progenics CIM project -- Active Biotech CD4 soluble -- Progenics CL 329753 -- Wyeth-Ayerst CD4, soluble -- Genzyme Transgenics CL22, Cobra -- ML Laboratories CD40 ligand -- Immunex CD4-ricin chain A -- Genentech Clenoliximab -- IDEC Clostridium difficile antibodies -- Epicyte CD59 gene therapy -- Alexion clotting factors -- Octagene CD8 TIL cell therapy -- Aventis Pasteur CD8, soluble -- Avidex CMB 401 -- Celltech CNTF -- Sigma-Tau CD95 ligand -- Roche Cocaine abuse vaccine - Cantab, CDP 571 -- Celltech CDP 850 - Celltech ImmuLogic, Scripps coccidiomycosis vaccine -- Arizo CDP 870 -- Celltech collagen -- Type I -- Pharming CDS-1 -- Ernest Orlando Collagen formation inhibitors -- FibroGen Cedelizumab -- Ortho-McNeil Cetermin -- Insmed

FIG. 1H

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Collagen/hydroxyapatite/bone growth factor CY 1747 -- Epimmune CY 1748 -- Epimmune -- Aventis Pasteur, Biopharm, Orquest Cyanovirin-N collagenase -- BioSpecifics Colorectal cancer vaccine - Wistar Institute Cystic fibrosis therapy -- CBR/IVAX Component B, Recombinant -- Serono CYT 351 Connective tissue growth factor inhibitors -- cytokine Traps -- Regeneron cytokines - Enzon, Cytoclonal FibroGen/Taisho Cytomegalovirus glycoprotein vaccine -Contortrostatin Chiron, Aguila Biopharmaceuticals, contraceptive vaccine -- Zonagen Contraceptive vaccine hCG Aventis Pasteur, Virogenetics Cytomegalovirus vaccine live -- Aventis Contraceptive vaccine male reversible --Pasteur IMMUCON Cytosine deaminase gene therapy --Contraceptive vaccine zona pellucida --GlaxoSmithKline Zonagen DA-3003 -- Dong-A Copper-64 labelled MAb TETA-1A3 -- NCI DAB389interleukin-6 -- Senetek Coraivne DAB389interleukin-7 Corsevin M DAMP^ -- Incyte Genomics C-peptide analogues -- Schwarz Daniplestim - Pharmacia CPI-1500 -- Consensus darbepoetin alfa -- Amgen CRF -- Neurobiological Tech. DBI-3019 -- Diabetogen cRGDfV pentapeptide – CRL 1095 -- CytRx DCC -- Genzyme DDF -- Hyseq CRL 1336 -- CvtRx decorin -- Integra, Telios CRL 1605 -- CytRx defensins -- Large Scale Biology CS-560 - Sankyo DEGR-VIIa CSF -- ZvmoGenetics Delmmunised antibody 3B6/22 AGEN CSF-G - Hangzhou, Dong-A, Hanmi Deimmunised anti-cancer antibodies --CSF-GM - Cangene, Hunan, LG Chem Biovation/Viragen CSF-M -- Zarix CT 1579 - Merck Frosst Dendroamide A Dengue vaccine -- Bavarian Nordic, Merck CT 1786 - Merck Frosst denileukin diftitox -- Ligand CT-112[^] -- BTG DES-1101 - Desmos CTB-134L - Xenova desirudin -- Novartis CTC-111 -- Kaketsuken desmopressin -- Unigene CTGF -- FibroGen Desmoteplase - Merck, Schering AG CTLA4-la -- Bristol-Myers Squibb Destabilase CTLA4-Ig gene therapy --Diabetes gene therapy - DeveloGen, Pfizer CTP-37 -- AVI BioPharma Diabetes therapy -- Crucell C-type natriuretic peptide -- Suntory Diabetes type 1 vaccine -- Diamyd CVS 995 - Corvas Intl. Therapeutics CX 397 - Nikko Kyodo

FIG. 11

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EGF-P64k vaccine -- Center of Molecular DiaCIM -- YM BioSciences dialytic oligopeptides - Research Corp **Immunology** Diamvd - Diamvd Therapeutics EL 246 -- LigoCyte DiaPep227-- Pepgen elastase inhibitor -- Synergen elcatonin --- Therapicon DiavaX – Corixa Diphtheria tetanus pertussis-hepatitis B EMD 72000 - Merck KGaA vaccine -- GlaxoSmithKline Emdogain -- BIORA emfilermin -- AMRAD DIR therapy -- Solis Therapeutics --Emoctakin -- Novartis DNase -- Genentech Dornase alfa -- Genentech enamel matrix protein -- BIORA Dornase alfa, inhalation -- Genentech Endo III -- NYU endostatin – EntreMed. Pharis Doxorubicin-anti-CEA MAb conjugate — Enhancins -- Micrologix Immunomedics DP-107 -- Trimeris Fnlimomab -- Isls Pharm. Enoxaparin sodium -- Pharmuka drotrecogin alfa -- Eli Lilly enzyme linked antibody nutrient depletion DTctGMCSF DTP-polio vaccine -- Aventis Pasteur therapy -- KS Biomedix Holdings DU 257-KM231 antibody conjugate --Eosinophil-derived neutralizing agent -EP-51216 -- Asta Medica Kvowa EP-51389 -- Asta Medica dural graft matrix - Integra EPH family ligands - Regeneron Duteplase – Baxter Intl. Epidermal growth factor -- Hitachi Kasei, DWP-401 -- Daewoong Johnson & Johnson DWP-404 -- Daewoong DWP-408 -- Daewoong Epidermal growth factor fusion toxin --E coli O157 vaccine - NiH Senetek Epidermal growth factor-genistein -E21-R -- BresaGen Eastern equine encephalitis virus vaccine - EPI-HNE-4 - Dyax EPI-KAL2 – Dvax Echicetin -Echinhibin 1 -Epoetin-alfa - Amgen, Dragon Pharmaceuticals, Nanjing Huaxin Echistatin -- Merck Fchitamine -Epratuzumab – Immunomedics EC-SOD -- PPL Therapeutics Epstein-Barr virus vaccine --EDF -- Alinomoto Eptacog alfa -- Novo Nordisk EDN derivative -- NIH Eptifibatide -- COR Therapeutics EDNA -- NIH Edobacomab -- XOMA erb-38 -Erlizumab -- Genentech Edrecolomab -- Centocor FF 5077

Efalizumab -- Genentech EGF fusion toxin - Seragen, Ligand Aviron/SmithKline Beecham, Bioresearch

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erythropoietin -- Alkermes, ProLease, Dong-Fas TR -- Human Genome Sciences Felvizumab - Scotgen A. Elanex. Genetics Institute, LG Chem. FFR-VIIa -- Novo Nordisk Protein Sciences, Serono, Snow Brand, FG-001 -- F-Gene SRC VB VECTOR, Transkaryotic FG-002 - F-Gene Therapies Erythropoietin Beta -- Hoffman La Roche FG-004 - F-Gene FG-005 - F-Gene Erythropoietin/Epoetin alfa -- Chugai FGF + fibrin -- Repair Escherichia coli vaccine -- North American Fibrimage -- Bio-Tech. General Vaccine, SBL Vaccin, Swiss Serum and fibrin-binding peptides - ISIS Innovation Vaccine Institute Berne fibrinogen -- PPL Therapeutics, Pharming etanercept -- Immunex fibroblast growth factor - Chiron, NYU, examorelin - Mediolanum Ramot, ZymoGenetics exonuclease VII fibrolase conjugate -- Schering AG F 105 -- Centocor Filgrastim -- Amgen F-992 -- Fomix filgrastim - PDA modified -- Xencor Factor IX - Alpha Therapeutics, Welfide Corp., CSL, enetics Institute/AHP, FLT-3 ligand -- Immunex Pharmacia, PPL Therapeutics FN18 CRM9 -Factor IX gene therapy -- Cell Genesys follistatin - Biotech Australia, Human Factor VII - Novo Nordisk, Bayer, Baxter Therapeutics follitropin alfa - Alkermes, ProLease, Intl. PowderJect, Serono, Akzo Nobel Factor VIIa - PPL Therapeutics, Follitropin Beta - Bayer, Organon ZymoGenetics Factor VIII - Bayer Genentech, Beaufour-FP 59 Ipsen, CLB, Inex, Octagen, Pharmacia, FSH -- Ferring FSH + LH -- Ferring Pharming Factor VIII -- PEGylated -- Bayer F-spondin -- CeNeS Factor VIII fragments -- Pharmacia fusion protein delivery system -- UAB Factor VIII gene therapy - Targeted Research Foundation fusion toxins - Boston Life Sciences Genetics Factor VIII sucrose formulation - Bayer, G 5598 -- Genentech GA-II - Transkaryotic Therapies Genentech Gamma-interferon analogues - SRC VB Factor VIII-2 -- Bayer VECTOR Factor VIII-3 - Bayer Factor Xa inhibitors - Merck, Novo Nordisk, Ganirelix -- Roche gastric lipase -- Meristem Mochida Factor XIII -- ZymoGenetics Gavilimomab – Factors VIII and IX gene therapy -- Genetics G-CSF - Amgen, SRC VB VECTOR GDF-1 -- CeNeS Institute/Targeted Genetics GDF-5 - Biopharm Famoxin -- Genset GDNF -- Amgen Fas (delta) TM protein - LXR BioTech.

FIG. 1K

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FIG. 1

gelsolin -- Biogen Gemtuzumab ozogamicin -- Celltech Gene-activated epoetin-alfa -- Aventis Pharma -- Transkarvotic Therapies Glanzmann thrombasthenia gene therapy -Glatiramer acetate -- Yeda glial growth factor 2 -- CeNeS GLP-1 - Amylin, Suntory, TheraTech, Watson GLP-1 peptide analogues – Zealand Pharaceuticals 4 1 glucagon -- Eli Lilly, ZymoGenetics Glucagon-like peptide-1 7-36 amide --Suntory Glucocerebrosidase -- Genzyme giutamate decarboxylase -- Genzyme Transgenics Glycoprotein S3 -- Kureha GM-CSF -- Immunex GM-CSF tumour vaccine -- PowderJect GnRH immunotherapeutic -- Protherics ap75 antigen -- ImClone ap96 -- Antigenics GPI 0100 -- Galenica GR 4991W93 -- GlaxoSmithKline Granulocyte colony-stimulating factor --Dong-A Granulocyte colony-stimulating factor conjugate grass allergy therapy -- Dynavax GRF1-44 -- ICN Growth Factor - Chiron, Atrigel, Atrix, Innogenetics, ZymoGenetics, Novo growth factor peptides -- Biotherapeutics growth hormone - LG Chem growth hormone, Recombinant human --GT 4086 -- Gliatech GW 353430 -- GlaxoSmithKline GW-278884 -- GlaxoSmithKline H 11 -- Viventia Biotech

Sciences haemoglobin -- Biopure haemoglobin 3011, Recombinant -- Baxter Healthcare haemoglobin crosfumaril – Baxter Intl. haemoglobin stabilized -- Ajinomoto haemoglobin, recombinant -- Apex HAF -- Immune Response Hantavirus vaccine HB 19 HBNF -- Regeneron HCC-1 -- Pharis hCG -- Milkhaus hCG vaccine -- Zonagen HE-317 -- Hollis-Eden Pharmaceuticals Heat shock protein cancer and influenza vaccines -- StressGen Helicobacter pylori vaccine -- Acambis, AstraZeneca/CSL, Chiron, Provalis Helistat-G -- GalaGen Hemolink -- Hemosol hepapoietin -- Snow Brand heparanase -- InSight heparinase I -- Ibex heparinase III - Ibex Hepatitis A vaccine -- American Biogenetic Sciences Hepatitis A vaccine inactivated Hepatitis A vaccine Nothav -- Chiron Hepatitis A-hepatitis B vaccine --GlaxoSmithKline hepatitis B therapy -- Tripep Hepatitis B vaccine - Amgen, Chiron SpA, Meiji Milk, NIS, Prodeva, PowderJect, Rhein Biotech Hepatitis B vaccine recombinant -- Evans Vaccines, Epitec Comblotech, Genentech, Medlmmune, Merck Sharp & Dohme, Rhein Biotech, Shantha Biotechnics, Vector, Yeda

H5N1 influenza A virus vaccine - Protein

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Hepatitis B vaccine recombinant TGP 943 -- HIV peptides -- American Home Products HIV vaccine - Applied bioTech., Axis Takeda Hepatitis C vaccine -- Bavarian Nordic. Genetics, Biogen, Bristol-Myers Squibb, Chiron, Innogenetics Acambis. Genentech, Korea Green Cross, NIS, Oncogen, Protein Sciences Corporation, Henatitis D vaccine -- Chiron Vaccines Terumo, Tonen Corporation, Wyeth-Hepatitis E vaccine recombinant --Averst, Wyeth-Lederle Vaccines-Malvern, Genelabs/GlaxoSmithKline, Novavax Advanced BioScience Laboratories. hepatocyte growth factor - Panorama, Bayarian Nordic, Bayarian Nordic/Statens Sosei hepatocyte growth factor kringle fragments -Serum Institute, GeneCure, Immune Response, Progenics, Therion Biologics, EntreMed Her-2/Neu peptides - Corixa United Biomedical, Chiron Herpes simplex glycoprotein DNA vaccine - HIV vaccine vCP1433 -- Aventis Pasteur HIV vaccine vCP1452 -- Aventis Pasteur Merck, Wyeth-Lederle Vaccines-Malvern, Genentech, GlaxoSmithKline, Chiron, HIV vaccine vCP205 -- Aventis Pasteur HL-9 -- American BioScience Takeda Herpes simplex vaccine -- Cantab HM-9239 -- Cytran HML-103 -- Hemosol Pharmaceuticals, CEL-SCI, Henderson HML-104 -- Hemosol Morley Herpes simplex vaccine live -- ImClone HML-105 -- Hemosol HML-109 -- Hemosol Systems/Wyeth-Lederle, Aventis Pasteur HGF derivatives -- Domne HMI -110 -- Hemosol HML-121 -- Hemosol hIAPP vaccine -- Crucell Hib-hepatitis B vaccine -- Aventis Pasteur hNLP -- Pharis Hookworm vaccine HIC 1 host-vector vaccines -- Henogen HIP-- Altachem Hirudins - Biopharma, Cangene, Dongkook, HPM 1 -- Chugai Japan Energy Corporation, Pharmacia HPV vaccine -- MediGene HSA - Meristem Corporation, SIR International, Sanofi-HSF - StressGen Synthelabo, Sotragene, Rhein Biotech HIV edible vaccine - ProdiGene HSP carriers --Weizmann, Yeda, Peptor HSPPC-70 -- Antigenics HIV ap120 vaccine - Chiron, Aiinomoto, HSPPC-96 -- pathogen-derived --GlaxoSmithKline, ID Vaccine, Progenics, VaxGen Antigenics HIV gp120 vaccine gene therapy -HSV 863 -- Novartis HIV gp160 DNA vaccine - PowderJect, HTLV-I DNA vaccine Aventis Pasteur, Oncogen, Hyland HTLV-I vaccine Immuno, Protein Sciences HTLV-II vaccine -- Access HU 901 -- Tanox HIV gp41 vaccine -- Panacos Hu23F2G -- ICOS HIV HGP-30W vaccine -- CEL-SCI HIV immune globulin - Abbott, Chiron HuHMFG1 FIG. 1M

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HuMax-II 15 -- Genmab Humal YM -- Intracell Human krebs statika -- Yamanouchi HYB 190 -- Hybridon HYB 676 — Hybridon human monoclonal antibodies --I-125 MAb A33 -- Celltech Abgenix/Biogen, Abgenix/ Corixa, Ibritumomab tiuxetan -- IDEC Abgenix/Immunex, Abgenix/Lexicon, Abgenix/ Pfizer, Athersys/Medarex, IBT-9401 -- Ibex Biogen/MorphoSys, CAT/Searle, IBT-9402 -- Ibex IC 14 - ICOS Centocor/Medarex, Corixa/Kirin Brewery, Corixa/Medarex, Eos BioTech./Medarex, Idarubicin anti-Ly-2.1 – IDEC 114 -- IDEC Fos/Xenerex, Exelixis/Protein Design IDEC 131 -- IDEC Labs. ImmunoGen/ Raven. IDEC 152 - IDEC Medarex/B. Twelve. IDM 1 -- IDM MorphoSys/ImmunoGen. XTL IDPS -- Hollis-Eden Pharmaceuticals Biopharmaceuticals/Dyax. iduronate-2-sulfatase -- Transkaryotic Human monoclonal antibodies --Medarex/Northwest Biotherapeutics. Therapies IGF/IBP-2-13 -- Pharis Medarex/Seattle Genetics IGN-101 -- Igeneon human netrin-1 -- Exelixis human papillomavirus antibodies -- Epicyte IK HIR02 -- Iketon Human papillomavirus vaccine -- Biotech IL-11 -- Genetics Institute/AHP IL-13-PE38 - NeoPharm Australia, IDEC, StressGen Human papillomavirus vaccine MEDI 501 - IL-17 receptor -- Immunex MedImmune/GlaxoSmithKline IL-18BP -- Yeda IL-1Hy1 -- Hyseq Human papillomavirus vaccine MEDI IL-1ß -- Celltech 503/MEDI 504 --IL-1ß adjuvant -- Celltech MedImmune/GlaxoSmithKline 11.-2 -- Chiron Human papillomavirus vaccine TA-CIN --II -2 + II -12 -- Hoffman La-Roche Cantab Pharmaceuticals Human papillomavirus vaccine TA-HPV --II -6/sII -6R fusion -- Hadasit Cantab Pharmaceuticals II -6R derivative -- Tosoh Human papillomavirus vaccine TH-GW --IL-7-Dap 389 fusion toxin -- Ligand IM-862 -- Cytran Cantab/GlaxoSmithKline human polyclonal antibodies - Biosite/Eos IMC-1C11 -- ImClone imiglucerase -- Genzyme BioTech./ Medarex Immune globulin intravenous (human) -human type II anti factor VIII monoclonal antibodies -- ThromboGenics Hoffman La Roche immune privilege factor -- Proneuron humanised anti glycoprotein lb murine Immunocal -- Immunotec monoclonal antibodies -- ThromboGenics Immunogene therapy - Briana Bio-Tech HumaRAD -- Intracell Immunoliposomal 5-fluorodeoxyuridine-HuMax EGFR -- Genmab dipalmitate --HuMax-CD4 -- Medarex FIG. 1N

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integrin antagonists - Merck immunosuppressant vaccine -- Aixlie interferon (Alpha2) -- SRC VB VECTOR, immunotoxin – Antisoma, NIH ImmuRAIT-Re-188 - Immunomedics Viragen, Dong-A, Hoffman La-Roche, Genentech imreg-1 - Imreg infertility -- Johnson & Johnson, E-TRANS interferon - BioMedicines, Human Genome Influenza virus vaccine -- Aventis Pasteur, Sciences Protein Sciences interferon (Alfa-n3)—Interferon Sciences inhibin -- Biotech Australia, Human Intl. interferon (Alpha), Biphasix -- Helix Therapeutics Inhibitory G protein gene therapy interferon (Alpha)-Amgen, BioNative, Novartis, Genzyme Transgenics, INKP-2001 -- InKine Hayashibara, Inhale Therapeutics Inolimomab -- Diaclone Systems, Medusa, Flamel, Dong-A, insulin -- AutoImmune, Altea, Biobras, BioSante, Bio-Tech. General, Chong Kun GeneTrol, Nastech, Shantha, Dang, Emisphere, Flamel, Provalis, Rhein Wassermann, LG Chem, Sumitomo, Aventis, Behring EGIS, Pepgen, Servier, Biotech, TranXenoGen insulin (bovine) -- Novartis Rhein Biotech. interferon (Alpha2A) insulin analogue -- Eli Lilly Insulin Aspart -- Novo Nordisk interferon (Alpha2B) - Enzon, Scheringinsulin detemir -- Novo Nordisk Plough, Biogen, IDEA interferon (Alpha-N1) -- GlaxoSmithKline insulin glargine -- Aventis insulin inhaled – Inhale Therapeutics interferon (beta) - Rentschler, GeneTrol, Meristem, Rhein Biotech, Toray, Yeda, Systems, Alkermes insulin oral -- Inovax Dajichi, Mochida insulin. AeroDose -- AeroGen interferon (Beta1A) – Serono, Biogen interferon (beta1A), inhale -- Biogen insulin, AERx -- Aradiam interferon (B1b)- Chiron insulin, BEODAS -- Elan interferon (tau) -- Pepgen insulin, Biphasix -- Helix insulin, buccal -- Generex Interferon alfacon-1 -- Amgen Interferon alpha-2a vaccine insulin, 12R -- Flemington insulin, intranasal -- Bentley Interferon Beta 1b -- Schering/Chiron, insulin, oral - Nobex, Unigene InterMune Interferon Gamma -- Boehringer Ingelheim, insulin, Orasome -- Endorex Sheffield, Rentschler, Havashibara insulin, ProMaxx -- Epic interferon receptor, Type I - Serono insulin, Quadrant -- Elan interferon(Gamma1B) - Genentech insulin, recombinant -- Aventis Interferon-alpha-2b + ribavirin - Biogen, insulin, Spiros - Elan insulin, Transfersome -- IDEA ICN insulin, Zymo, recombinant -- Novo Nordisk Interferon-alpha-2b gene therapy --Schering-Plough insulinotropin -- Scios Interferon-con1 gene therapy insulvsin gene therapy -

FIG. 10

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IPF -- Metabolex interleukin-1 antagonists -- Dompe IR-501 -- Immune Response Interleukin-1 receptor antagonist -- Abbott ISIS 9125 -- Isis Pharmaceuticals Bioresearch, Pharmacia Interleukin-1 receptor type I -- Immunex ISURF No. 1554 — Millennium ISURF No. 1866 - Iowa State Univer. interleukin-1 receptor Type II -- Immunex Interleukin-10 - DNAX, Schering-Plough ITF-1697 - Italfarmaco IxC 162 -- Ixion Interleukin-10 gene therapy interleukin-12 -- Genetics Institute, Hoffman J 695 -- Cambridge Antibody Tech., Genetics Inst., Knoll La-Roche interleukin-13 -- Sanofi Jagged + FGF -- Repair interleukin-13 antagonists -- AMRAD JKC-362 -- Phoenix Pharmaceuticals JTP-2942 - Japan Tobacce Interleukin-13-PE38QQR Juman monoclonal antibodies -interleukin-15 -- Immunex Medarex/Raven interleukin-16 -- Research Corp K02 -- Axvs Pharmaceuticals interleukin-18 -- GlaxoSmithKline Keliximab -- IDEC Interleukin-1-alpha -- Immunex/Roche Keyhole limpet haemocyanin interleukin-2 - SRC VB VECTOR, Alinomoto, Biomira KGF - Amgen KM 871 -- Kyowa Interleukin-3 -- Cangene KPI 135 -- Scios Interleukin-4 -- Immunology Ventures, KPI-022 -- Scios Sanofi Winthrop, Schering-Plough, Immunex/ Sanofi Winthrop, Bayer, Ono Kringle 5 KSB 304 Interleukin-4 + TNF-Alpha -- NIH KSB-201 -- KS Biomedix interleukin-4 agonist -- Bayer interleukin-4 fusion toxin -- Ligand L 696418 - Merck Interleukin-4 receptor - Immunex, Immun L 703801 -- Merck L1 -- Acorda Interleukin-6 - Alinomoto, Cangene, Yeda, Genetics Institute. Novartis L-761191 -- Merck lactoferrin - Meristem, Pharming, Agennix interleukin-6 fusion protein interleukin-6 fusion toxin - Ligand, Serono lactoferrin cardio -- Pharming LAG-3 -- Serono interleukin-7 - IC Innovations LAIT -- GEMMA interleukin-7 receptor -- Immunex LAK cell cytotoxin -- Arizona interleukin-8 antagonists -- Kyowa lamellarins - PharmaMar/University of Hakko/Millennium/Pfizer interleukin-9 antagonists -- Genaera Malaga interleukins -- Cel-Sci Jaminin A peptides -- NIH lodine I 131 tositumomab -- Corixa lanoteplase -- Genetics Institute ior EPOCIM -- Center of Molecular laronidase -- BioMarin Lassa fever vaccine Immunology LCAT -- NIH lor-P3 -- Center of Molecular Immunology LDP 01 -- Millennium IP-10 -- NIH

FIG. 1P

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Lyme disease vaccine -- Aquila LDP 02 -- Millennium Biopharmaceuticals, Aventis, Pasteur, Lecithinized superoxide dismutase --Symbicom, GlaxoSmithKline, Hyland Seikagaku LeIF adiuvant --- Corixa Immuno, Medimmune Lymphocytic choriomeningitis virus vaccine leishmaniasis vaccine -- Corixa lymphoma vaccine - Biomira, Genitope lenercept -- Hoffman La-Roche LYP18 Lenograstim - Aventis, Chugai lys plasminogen, recombinant lepirudin -- Aventis Lysosomal storage disease gene therapy -leptin - Amgen, IC Innovations Leptin gene therapy -- Chiron Corporation Avigen lysostaphin -- Nutrition 21 leptin, 2nd-generation -- Amgen M 23 -- Gruenenthal leridistim -- Pharmacia M1 monocional antibodies -- Acorda leuprolide, ProMaxx -- Epic Therapeutics leuprorelin, oral -- Unigene MA 16N7C2 – Corvas Intl. LeuTech -- Papatin malaria vaccine -- GlaxoSmithKline. LEX 032 -- SuperGen AdProTech, Antigenics, Apovia, Aventis LiDEPT -- Novartis Pasteur, Axis Genetics, Behringwerke, lipase -- Altus Biologics CDCP. Chiron Vaccines, Genzyme lipid A vaccine -- EntreMed Transgenics, Hawaii, MedImmune, NIH, lipid-linked anchor Tech. - ICRT, ID NYU, Oxxon, Roche/Saramane, Biotech Biomedical liposome-CD4 Tech. --- Sheffield Australia, Rx Tech Malaria vaccine CDC/NIIMALVAC-1 Listeria monocytogenes vaccine malaria vaccine, multicomponent I MB 1 mammaglobin -- Corixa LMB 7 LMB 9 -- Battelle Memorial Institute. NIH mammastatin -- Biotherapeutics mannan-binding lectin -- Natlmmu LM-CD45 -- Cantab Pharmaceuticals mannan-MUC1 -- Psiron Iovastatin -- Merck MAP 30 LSA-3 Marinovir -- Phytera LT-ß receptor -- Biogen lung cancer vaccine - Corixa MARstem -- Maret MB-015 - Mochida lusupultide -- Scios MBP -- ImmuLogic L-Vax -- AVAX MCI-028 -- Mitsubishi-Tokyo LY 355455 -- Eli Lilly MCIF -- Human Genome Sciences LY 366405 -- Eli Lilly MDC -- Advanced BioScience -- Akzo LY-355101 -- Eli Lilly Lyme disease DNA vaccine - Vical/Aventis Nobel, ICOS MDX 11 -- Medarex Pasteur MDX 210 -- Medarex

> MDX 22 -- Medarex MDX 22

FIG. 1Q

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Methionine lyase gene therapy --MDX 240 -- Medarex MDX 33 AntiCancer Met-RANTES - Genexa Biomedical, MDX 44 -- Medarex Serono MDX 447 -- Medarex Metreleptin MDX H210 - Medarex MGDF -- Kirin MDX RA -- Houston BioTech., Medarex ME-104 -- Pharmexa MGV -- Progenics micrin - Endocrine Measles vaccine microplasmin -- ThromboGenics Mecasermin -- Cephalon/Chiron, Chiron MIF -- Genetics Institute MEDI 488 -- Medimmune migration inhibitory factor -- NIH MEDI 500 Mim CD4.1 – Xvcte Therapies MEDI 507 -- BioTransplant mirostipen - Human Genome Sciences melanin concentrating hormone ---Neurocrine Biosciences MK 852 -- Merck Mobenakin -- NIS melanocortins -- OMRF Melanoma monoclonal antibodies -- Viragenmolgramostim -- Genetics Institute, Novartis monoclonal antibodies -- Abgenix/Celltech, melanoma vaccine -- GlaxoSmithKline. Immusol/ Medarex, Viragen/ Roslin Akzo Nobel, Avant, Aventis Pasteur, Institute, Cambridge Antibody Tech./Elan Bayarian Nordic, Biovector, CancerVax, Genzyme Molecular Oncology, Humbolt, MAb 108 -ImClone Systems, Memorial, NYU, Oxxon MAb 10D5 --MAb 14.18-interleukin-2 immunocytokine --Melanoma vaccine Magevac -- Therion memory enhancers - Scios Lexiaen MAb 14G2a -meningococcal B vaccine -- Chiron meningococcal vaccine -- CAMR MAb 15A10 -Meningococcal vaccine group B conjugate - MAb 170 -- Biomira North American Vaccine MAb 177Lu CC49 --Meningococcal vaccine group B MAb 17F9 MAb 1D7 recombinant - BioChem Vaccines. MAb 1F7 - Immune Network Microscience Meningococcal vaccine group Y conjugate - MAb 1H10-doxorubicin conjugate MAb 26-2F - North American Vaccine Meningococcal vaccine groups A B and C MAb 2A11 MAh 2E1 -- RW Johnson conjugate -- North American Vaccine MAb 2F5 Mepolizumab -- GlaxoSmithKline MAb 31.1 -- International BioImmune Metastatin - EntreMed, Takeda Met-CkB7 -- Human Genome Sciences Systems MAb 32 - Cambridge Antibody Tech., met-enkephalin -- TN! MFTH-1 -- Human Genome Sciences Peptech MAb 323A3 — Centocor methioninase -- AntiCancer

FIG. 1R

MAb 3C5

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MAb C242-PE conjugate MAb 3F12 MAb 3F8 MAb c30-6 MAb CA208-cytorhodin-S conjugate ---MAb 42/6 MAb 425 - Merck KGaA Hoechst Japan MAb 447-52D - Merck Sharp & Dohme MAb CC49 -- Enzon MAb 45-2D9- - haematoporphyrin MAb ch14.18 -MAb CH14.18-GM-CSF fusion protein conjugate MAb 4B4 Lexigen MAb 4E3-CPA conjugate -- BCM Oncologia MAb chCE7 MAb CI-137 -- AMRAD MAb 4E3-daunorubicin conjugate MAb cisplatin conjugate MAb 50-6 MAb 50-61A - Institut Pasteur MAb Cl.B-CD19 MAb CLB-CD19v MAb 5A8 --- Biogen MAb 791T/36-methotrexate conjugate MAb CLL-1 -- Peregrine MAb CLL-1-GM-CSF conjugate MAb 7c11.e8 MAb CLL-1-IL-2 conjugate -- Peregrine MAb 7E11 C5-selenocystamine conjugate MAb 93KA9 -- Novartis MAb CLN IgG -- doxorubicin conjugates MAb A5B7-cisplatin conjugate --MAb conjugates - Tanox Biodynamics Research, Pharmacia MAh D612 MAb Dal B02 MAb A5B7-I-131 MAb DC101 -- ImClone MAb A7 MAb EA 1 -MAb A717 -- Exocell MAb EC708 - Biovation MAb A7-zinostatin conjugate MAb ABX-RB2 - Abgentx MAb EP-5C7 -- Protein Design Labs MAb ERIC-1 -- ICRT MAh ACA 11 MAh AFP-I-131 - Immunomedics MAb F105 gene therapy MAb FC 2.15 MAb AP1 MAb G250 -- Centocor MAb AZ1 MAb B3-LvsPE40 conjugate MAb GA6 MAb GA733 MAb B4 – United Biomedical MAb Gliomab-H -- Viventia Biotech MAb B43 Genistein-conjugate MAb HB2-saporin conjugate MAb B43.13-Tc-99m -- Biomira MAb B43-PAP conjugate MAb HD 37 -MAb B4G7-gelonin conjugate MAb HD37-ricin chain-A conjugate MAb BCM 43-daunorubicin conjugate --MAb HNK20 -- Acambis MAb huN901-DM1 conjugate -BCM Oncologia MAb BIS-1 ImmunoGen MAb BMS 181170 - Bristol-Myers Squibb MAb I-131 CC49 - Corixa MAb ICO25 MAb BR55-2 MAb ICR12-CPG2 conjugate MAb BW494

MAb C 242-DM1 conjugate -- ImmunoGen MAb ICR-62

FIG. 1S

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MAb IRac-ricin A conjugate MAb R-24 MAh R-24 a Human GD3 -- Celltech MAb K1 MAb RFB4-ricin chain A conjugate MAb KS1-4-methotrexate conjugate MAb RFT5-ricin chain A conjugate MAb L6 -- Bristol-Myers Squibb, Oncogen MAb SC 1 MAb LiCO 16-88 MAb SM-3 -- ICRT MAb LI 2-I-131 - Immunomedics MAb SMART 1D10 -- Protein Design Labs MAb LL2-Y-90 MAb SMART ABL 364 -- Novartis MAb LS2D617 -- Hybritech MAb SN6f MAb LYM-1-gelonin conjugate MAb SN6f-deglycosylated ricin A chain MAb LYM-1-I-131 MAb LYM-1-Y-90 conjugate -MAb SN6i MAb LYM-2 -- Peregrine MAb SN7-ricin chain A conjugate MAb M195 MAb T101-Y-90 conjugate -- Hybritech MAb M195-bismuth 213 conjugate --MAb T-88 - Chiron Protein Design Labs MAb M195-gelonin conjugate MAb TB94 -- Cancer ImmunoBiology MAb TEC 11 MAb M195-I-131 MAb TES-23 -- Chugai MAh M195-Y-90 MAb TM31 -- Avant MAb MA 33H1 -- Sanofi MAb TNT-1 -- Cambridge Antibody Tech., MAb MAD11 MAb MGb2 Peregrine MAb TNT-3 MAb MINT5 MAb TNT-3 -- IL2 fusion protein -.MAb MK2-23 MAb MOC31 ETA(252-613) conjugate MAb TP3-At-211 MAb TP3-PAP conjugate -MAb MOC-31-In-111 MAb MOC-31-PE conjugate MAb UJ13A -- ICRT MAb UN3 MAb MR6 -MAb ZME-018-gelonin conjugate MAb MRK-16 -- Aventis Pasteur MAb-BC2 -- GlaxoSmithKline MAh MS11G6 MAb-DM1 conjugate -- ImmunoGen MAh MX-DTPA BrE-3 MAb-ricin-chain-A conjugate -- XOMA MAb MY9 MAb-temoporfin conjugates MAb Nd2 -- Tosoh Monopharm C -- Viventia Biotech MAb NG-1 -- Hygeia monteplase -- Eisai MAb NM01 - Nissin Food montirelin hydrate -- Gruenenthal MAb OC 125 MAb OC 125-CMA conjugate moroctocog alfa -- Genetics Institute MAb OKI-1 -- Ortho-McNeil Moroctocog-alfa -- Pharmacia MP 4 MAb OX52 -- Bioproducts for Science MP-121 -- Biopharm MAb PMA5 MP-52 - Biopharm MAb PR1

FIG. 1T

MAb prost 30

MRA -- Chugai

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Neuroprotective vaccine -- University of MS 28168 -- Mitsui Chemicals, Nihon Auckland Scherina neurotrophic chimaeras -- Regeneron MSH fusion toxin -- Ligand neurotrophic factor - NsGene, CereMedix MSI-99 -- Genaera MT 201 -- Micromet NeuroVax -- Immune Response neurturin -- Genentech Muc-1 vaccine -- Corixa neutral endopeptidase -- Genentech mucosal tolerance - Aberdeen NGF enhancers -- NeuroSearch mullerian inhibiting subst NHL vaccine -- Large Scale Biology muplestim -- Genetics Institute. Novartis. NIP45 -- Boston Life Sciences DSM Anti-Infectives NKI-R20 murine MAb -- KS Biomedix Mutant somatropin -- JCR Pharmaceutical NM 01 - Nissin Food NMI-139 -- NitroMed MV 833 -- Toagosei Mycoplasma pulmonis vaccine NMMP -- Genetics Institute Mycoprex - XOMA NN-2211 -- Novo Nordisk myeloperoxidase -- Henogen Nogain -- Regeneron myostatin -- Genetics Institute Nonacog alfa Nacolomab tafenatox -- Pharmacia Norelin -- Biostar nagrestipen - British Biotech Norwalk virus vaccine NRLU 10 -- NeoRx NAP-5 - Corvas Intl. NRLU 10 PE -- NeoRx NAPc2 - Corvas Intl. NT-3 -- Regeneron nartograstim - Kyowa Natalizumab -- Protein Design Labs NT-4/5 - Genentech NU 3056 Nateplase - NIH, Nihon Schering nateplase -- Schering AG NU 3076 NX 1838 -- Gilead Sciences NBI-3001 - Neurocrine Biosci. NY ESO-1/CAG-3 antigen -- NIH NRI-5788 - Neurocrine Biosci. NYVAC-7 -- Aventis Pasteur NBI-6024 -- Neurocrine Biosci. NZ-1002 -- Novazyme Nef inhibitors -- BRI Neisseria gonorrhoea vaccine - Antex obesity therapy -- Nobex Biologics OC 10426 -- Ontogen Neomycin B-arginine conjugate OC 144093 -- Ontogen OCIF -- Sankvo Nerelimomab -- Chiron Oct-43 - Otsuka Nerve growth factor - Amgen - Chiron, OK PSA - liposomal Genentech OKT3-gamma-1-ala-ala Nerve growth factor gene therapy OM 991 nesiritide citrate -- Scios OM 992 neuregulin-2 -- CeNeS neurocan -- NYU Omalizumab -- Genentech neuronal delivery system -- CAMR oncoimmunin-L -- NIH

FIG. 1U

Oncolvsin B - ImmunoGen

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Oncolvsin CD6 -- ImmunoGen Oncolvsin M -- ImmunoGen Oncolvsin S -- ImmunoGen Oncophage -- Antigenics Oncostatin M -- Bristol-Myers Squibb OncoVax-CL -- Jenner Biotherapies OncoVax-P -- Jenner Biotherapies onercept -- Yeda onychomycosis vaccine -- Boehringer Ingelheim opebecan -- XOMA opioids -- Arizona Opreivekin -- Genetics Institute Org-33408 b-- Akzo Nobel Orolip DP -- EpiCept orvzacvstatin OSA peptides - GenSci Regeneration osteoblast-cadherin GF -- Pharis Osteocalcin-thymidine kinase gene therapy PEG anti-ICAM MAb -- Boehringer osteogenic protein -- Curis osteopontin - OraPharma osteoporosis peptides - Integra, Telios osteoprotegerin - Amgen, SnowBrand otitis media vaccines -- Antex Biologics ovarian cancer -- University of Alabama OX40-IgG fusion protein -- Cantab, Xenova P 246 -- Diatide P 30 -- Alfacell p1025 -- Active Biotech P-113[^] -- Demegen P-16 peptide -- Transition Therapeutics p43 -- Ramot P-50 peptide -- Transition Therapeutics p53 + RAS vaccine -- NIH, NCI PACAP(1-27) analogue paediatric vaccines -- Chiron Pafase -- ICOS PAGE-4 plasmid DNA -- IDEC PAI-2 -- Biotech Australia, Human Therapeutics Palivizumab -- Medimmune

PAM 4 -- Merck pamiteplase -- Yamanouchi pancreatin, Minitabs -- Eurand Pangen -- Fournier Pantarin - Selective Genetics Parainfluenza virus vaccine – Pharmacia. Pierre Fabre paraoxanase - Esperion parathyroid hormone - Abiogen, Korea Green Cross Parathyroid hormone (1-34) --Chugai/Suntory Parkinson's disease gene therapy -- Cell Genesys/ Ceregene Parvovirus vaccine -- MedImmune PCP-Scan – Immunomedics PDGF cocktail -- Theratechnologies peanut allergy therapy -- Dynavax Ingelheim PEG asparaginase – Enzon PEG alucocerebrosidase PEG hirudin - Knoll PEG interferon-alpha-2a -- Roche PEG interferon-alpha-2b + ribavirin -Biogen, Enzon, ICN Pharmaceuticals. Schering-Piough PEG MAb A5B7 --Pegacaristim - Amgen -- Kirin Brewery --ZvmoGenetics Pegaldesleukin – Research Corp pegaspargase -- Enzon pegfilgrastim -- Amgen PEG-interferon Alpha -- Viragen PEG-interferon Alpha 2A -- Hoffman La-Roche PEG-interferon Alpha 2B -- Schering-Plough PEG-r-hirudin -- Abbott PFG-uricase -- Mountain View Pegvisomant – Genentech

FIG. 1V

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PEGylated proteins, PolyMASC -- Valentis Pharmaprojects No. 5947 -- StressGen PEGylated recombinant native human leptin Pharmaprojects No. 5961 --Theratechnologies - Roche Pharmaprojects No. 5962 -- NIH Pemtumomab Pharmaprojects No. 5966 -- NIH Penetratin -- Cyclacel Pharmaprojects No. 5994 -- Pharming Pepscan - Antisoma Pharmaprojects No. 5995 -- Pharming peptide G - Peptech, ICRT Pharmaprojects No. 6023 -- IMMUCON peptide vaccine -- NIH .NCI Pharmaprojects No. 6063 -- Cytoclonal Pexelizumab pexiganan acetate -- Genaera Pharmaprojects No. 6073 - SIDDCO Pharmaprojects No. 6115 - Genzyme Pharmaprojects No. 3179 -- NYU Pharmaprojects No. 3390 - Ernest Orlando Pharmaprojects No. 6227 - NIH Pharmaprojects No. 6230 - NIH Pharmaprojects No. 3417 -- Sumitomo Pharmaprojects No. 6236 - NIH Pharmaprojects No. 3777 -- Acambis Pharmaprojects No. 6243 -- NIH Pharmaprojects No. 4209 -- XOMA Pharmaprojects No. 4349 - Baxter Intl. Pharmaprojects No. 6244 -- NIH Pharmaprojects No. 6281 -- Senetek Pharmaprojects No. 4651 Pharmaprojects No. 4915 -- Avanir Pharmaprojects No. 6365 - NIH Pharmaprojects No. 5156 -- Rhizogenics Pharmaprojects No. 6368 - NIH Pharmaprojects No. 6373 -- NIH Pharmaprojects No. 5200 - Pfizer Pharmaprojects No. 6408 - Pan Pacific Pharmaprojects No. 5215 -- Origene Pharmaprojects No. 6410 -- Athersys Pharmaprojects No. 5216 -- Origene Pharmaprojects No. 5218 -- Origene Pharmaprojects No. 6421 - Oxford Pharmaprojects No. 5267 -- ML GlycoSciences Pharmaprojects No. 6522 -- Maxygen I aboratories Pharmaprojects No. 6523 -- Pharis Pharmaprojects No. 5373 -- MorphoSys Pharmaprojects No. 6538 - Maxygen Pharmaprojects No. 5493 -- Metabolex Pharmaprojects No. 6554 - APALEXO Pharmaprojects No. 5707 - Genentech Pharmaprojects No. 6560 - Ardana Pharmaprojects No. 5728 -- Autogen Pharmaprojects No. 5733 -- BioMarin Pharmaprojects No. 6562 -- Bayer Pharmaprojects No. 6569 - Eos Pharmaprojects No. 5757 - NIH Phenoxazine Pharmaprojects No. 5765 --- Gryphon Pharmaprojects No. 5830 -- AntiCancer Phenylase -- Ibex Pigment epithelium derived factor -Pharmaprojects No. 5839 -- Dyax plasminogen activator inhibitor-1, Pharmaprojects No. 5849 -- Johnson & recombinant -- DuPont Pharmaceuticals .lohnson Pharmaprojects No. 5860 -- Mitsubishi-Tokyo

Pharmaprojects No. 5869 - Oxford

Pharmaprojects No. 5883 -- Asahi Brewery

GlycoSciences

FIG. 1W

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prostate-specific antigen -- EntreMed Plasminogen activators -- Abbott protein A -- RepliGen Laboratories, American Home Products, protein adhesives -- Enzon Boehringer Mannheim, Chiron Corporation, DuPont Pharmaceuticals, Eli protein C - Baxter Intl., PPL Therapeutics, Lilly, Shionogi, Genentech, Genetics ZymoGenetics protein C activator - Gilead Sciences Institute, GlaxoSmithKline, Hemispherx Biopharma, Merck & Co, Novartis, protein kinase R antags -- NIH Pharmacia Corporation, Wakamoto, Yeda protirelin - Takeda plasminogen-related peptides -- Bio-Tech. protocadherin 2 -- Caprion Pro-urokinase - Abbott, Bristol-Myers General/MGH Squibb, Dainippon, Tosoh -- Welfide platelet factor 4 – RepliGen P-selectin alycoprotein ligand-1 -- Genetics Platelet-derived growth factor - Amgen --Institute ZvmoGenetics pseudomonal infections -- InterMune plusonermin-Hayashibara Pseudomonas vaccine -- Cytovax PMD-2850 -- Protherics PSGL-Ig -- American Home Products Pneumococcal vaccine - Antex Biologics, PSP-94 -- Procyon Aventis Pasteur Pneumococcal vaccine intranasal --PTH 1-34 -- Nobex BioChem Vaccines/Biovector Quilimmune-M -- Antigenics R 101933 PR1A3 R 125224 -- Sankvo PR-39 RA therapy -- Cardion pralmorelin -- Kaken Rables vaccine recombinant -- Aventis Pretarget-Lymphoma -- NeoRx Pasteur, BioChem Vaccines, Kaketsuken Priliximab -- Centocor **Pharmaceuticals** PRO 140 -- Progenics RadioTheraCIM -- YM BioSciences PRO 2000 -- Procept Ramot project No. 1315 -- Ramot PRO 367 - Progenics Ramot project No. K-734A -- Ramot PRO 542 -- Progenics Ramot project No. K-734B -- Ramot pro-Apo A-I -- Esperion RANK - Immunex prolactin -- Genzyme Prosaptide TX14(A) -- Bio-Tech. General ranpirnase -- Alfacell ranpirnase-anti-CD22 MAb -- Alfacell prostate cancer antbodies - Immunex, RANTES inhibitor -- Milan UroCor RAPID drug delivery systems -- ARIAD prostate cancer antibody therapy -rasburicase -- Sanofi Genentech/UroGenesys, rBPI-21, topical -- XOMA Genotherapeutics prostate cancer immunotherapeutics -- The RC 529 -- Corixa rCFTR -- Genzyme Transgenics PSMA Development Company prostate cancer vaccine - Aventis Pasteur, RD 62198 rDnase - Genentech Zonagen, Corixa, Dendreon, Jenner RDP-58 -- SangStat Biotherapies, Therion Biologics FIG. 1X

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Ribozyme gene therapy -- Genset RecepTox-Fce -- Keryx Rickettsial vaccine recombinant RecepTox-GnRH - Keryx, MTR RIGScan CR -- Neoprobe Technologies RIP-3 -- Rigel RecepTox-MBP - Keryx, MTR RK-0202 -- RxKinetix Technologies RLT peptide -- Esperion recFSH -- Akzo Nobel, Organon rM/NEI -- IVAX REGA 3G12 mCRP -- Immtech Regavirumab -- Teijin relaxin - Connetics Corp RN-1001 - Renovo RN-3 -- Renovo Renal cancer vaccine -- Macropharm repifermin -- Human Genome Sciences RNAse conjugate -- Immunomedics Respiratory syncytial virus PFP-2 vaccine - RO 631908 - Roche Rotavirus vaccine -- Merck Wyeth-Lederle RP 431 -- DuPont Pharmaceuticals Respiratory syncytial virus vaccine -GlaxoSmithKline, Pharmacia, Pierre Fabre RP-128 -- Resolution Respiratory syncytial virus vaccine RPE65 gene therapy --RPR 110173 -- Aventis Pasteur inactivated RPR 115135 -- Aventis Pasteur Respiratory syncytial virus-parainfluenza RPR 116258A - Aventis Pasteur virus vaccine -- Aventis Pasteur. rPSGL-Ig -- American Home Products Pharmacia Reteplase -- Boehringer Mannheim, r-SPC surfactant -- Byk Gulden Hoffman La-Roche rV-HER-2/neu -- Therion Biologics SA 1042 -- Sankvo Retropep -- Retroscreen sacrosidase - Orphan Medical RFB4 (dsFv) PE38 RFI 641 - American Home Products Sant 7 Sargramostim -- Immunex RFTS -- UAB Research Foundation saruplase -- Gruenenthal RG 12986 -- Aventis Pasteur Satumomab -- Cytogen RG 83852 - Aventis Pasteur SB 1 -- COR Therapeutics RG-1059 - RepliGen SB 207448 -- GlaxoSmithKline rGCR - NIH SB 208651 -- GlaxoSmithKline rGLP-1 -- Restoragen SB 240683 — GlaxoSmithKline rGRF -- Restoragen SB 249415 -- GlaxoSmithKline rh Insulin – Eli Lilly RHAMM targeting peptides -- Cangene SB 249417 - GlaxoSmithKline SB 6 — COR Therapeutics rHb1.1 - Baxter Intl. rhCC10 - Claragen SB RA 31012 -SC 56929 - Pharmacia rhCG -- Serono SCA binding proteins - Curis, Enzon Rheumatoid arthritis gene therapy scFv(14E1)-ETA Berlex Laboratories, Rheumatoid arthritis vaccine -- Veterans Schering AG Affairs Medical Center ScFv(FRP5)-ETA rhLH - Serono

FIG. 1Y

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ScFv6C6-PE40 --SCH 55700 -- Celltech Schistosomiasis vaccine -- Glaxo Wellcome/Medeva, Brazil SCPF -- Advanced Tissue Sciences scuPA-suPAR complex -- Hadasit SD-9427 -- Pharmacia SDF-1 -- Ono SDZ 215918 -- Novartis SDZ 280125 -- Novartis SDZ 89104 -- Novartis SDZ ABL 364 -- Novartis SDZ MMA 383 - Novartis serine protease inhibs - Pharis sermorelin acetate -- Serono SERP-1 -- Viron sertenef -- Dainippon serum albumin, Recombinant human --Aventis Behring serum-derived factor -- Hadasit Sevirumab -- Novartis SGN 14 -- Seatle Genetics SGN 15 -- Seatle Genetics SGN 17/19 - Seatle Genetics SGN 30 -- Seatle Genetics SGN-10 -- Seatle Genetics SGN-11 -- Seatle Genetics SH 306 - DuPont Pharmaceuticals Shanvac-B - Shantha Shigella flexneri vaccine - Avant, Acambis, Novavax Shigella sonnei vaccine -sICAM-1 -- Boehringer Ingelheim Silteplase -- Genzyme SIV vaccine -- Endocon, Institut Pasteur SK 896 -- Sanwa Kagaku Kenkyusho SK-827 -- Sanwa Kagaku Kenkyusho Skeletex -- CellFactors SKF 106160 - GlaxoSmithKline S-nitroso-AR545C --SNTP -- Active Biotech

somatomedin-1 - GroPep, Mitsubishi-Tokyo, NIH somatomedin-1 carrier protein -- Insmed somatostatin -- Ferring Somatotropin/ Human Growth Hormone -- Bio-Tech. General, Eli Lilly somatropin -- Bio-Tech. General, Alkermes, ProLease, Aventis Behring, Biovector, Cangene, Dong-A, Eli Lilly, Emisphere, Enact, Genentech, Genzyme Transgenics, Grandis/InfiMed, CSL, InfiMed, MacroMed, Novartis, Novo Nordisk, Pharmacia Serono, TranXenoGen somatropin derivative -- Schering AG somatropin, AIR -- Eli Lilly Somatropin, inhaled -- Eli Lilly/Alkermes somatropin, Kabi -- Pharmacia somatropin, Orasome -- Novo Nordisk Sonermin - Dainippon Pharmaceutical SP(V5,2)C -- Supertek SPf66 sphingomyelinase -- Genzyme SR 29001 -- Sanofi SR 41476 -- Sanofi SR-29001 -- Sanofi SS1(dsFV)-PE38 -- NeoPharm ß2 microalobulin – Avidex ß2-microglobulin fusion proteins -- NIH ß-amyloid peptides -- CeNeS ß-defensin -- Pharis Staphylococcus aureus infections --Inhibitex/ZLB Staphylococcus aureus vaccine conjugate --Nabi Staphylococcus therapy - Tripep Staphylokinase - Biovation, Prothera. Thrombogenetics Streptococcal A vaccine -- M6 Pharmaceuticals, North American Vaccine Streptococcal B vaccine -- Microscience

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Streptococcal B vaccine recombinant --TFPI - EntreMed Biochem Vaccines taD-IL-2 - Takeda TGF-Alpha -- ZymoGenetics Streptococcus pyogenes vaccine TGF-B -- Kolon STRL-33 -- NIH TGF-B2 -- Insmed Subalin -- SRC VB VECTOR TGF-ß3 -- OSI SUIS -- United Biomedical Thalassaemia gene therapy -- Crucell SUIS-LHRH -- United Biomedical TheraCIM-h-R3 — Center of Molecular SUN-E3001 -- Suntory super high affinity monoclonal antibodies -Immunology, YM BioSciences Theradigm-HBV -- Epimmune YM BioSciences Theradiam-HPV -- Epimmune Superoxide dismutase – Chiron, Enzon, Theradigm-malaria -- Epimmune Ube Industries, Bio-Tech, Yeda Theradigm-melanoma – Epimmune superoxide dismutase-2 -- OXIS TheraFab - Antisoma suppressin - UAB Research Foundation ThGRF 1-29 - Theratechnologies SY-161-P5 -- ThromboGenics ThGRF 1-44 -- Theratechnologies SY-162 -- ThromboGenics Systemic lupus erythematosus vaccine -thrombomodulin – Iowa, Novocastra Thrombopoietin -- Dragon Pharmaceuticals. MedClone/VivoRx Genentech T cell receptor peptide vaccine thrombopoietin, Pliva -- Receptron T4N5 liposomes -- AGI Dermatics TACI, soluble - ZymoGenetics Thrombospondin 2 – targeted apoptosis -- Antisoma thrombostatin - Thromgen thymalfasin -- SciClone tasonermin -- Boehringer Ingelheim thymocartin - Gedeon Richter TASP thymosin Alpha1 -- NIH TASP-V thyroid stimulating hormone - Genzyme Tat peptide analogues -- NIH tICAM-1 - Bayer TBP 1 -- Yeda Tick anticoagulant peptide -- Merck TBP !! TBV25H -- NIH TIF -- Xoma Tc 99m ior cea1 -- Center of Molecular Tifacogin – Chiron, NIS, Pharmacia Tissue factor -- Genentech **Immunology** Tissue factor pathway inhibitor Tc 99m P 748 -- Diatide Tc 99m votumumab -- Intracell TJN-135 -- Tsumura TM 27 - Avant Tc-99m rh-Annexin V - Theseus Imaging TM 29 -- Avant teceleukin -- Biogen tenecteplase -- Genentech TMC-151 – Tanabe Seiyaku TNF tumour necrosis factor -- Asahi Kasei Teriparatide -- Armour Pharmaceuticals, TNF Alpha -- Cytlmmune Asahi Kasei, Eli Lilly TNF antibody -- Johnson & Johnson terlipressin - Ferring testisin -- AMRAD TNF binding protein -- Amgen TNF degradation product -- Oncotech Tetrafibricin -- Roche

FIG. 1AA

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TXU-PAP TNF receptor -- Immunex TNF receptor 1, soluble -- Amgen TY-10721 - TOA Eivo TNF Tumour necrosis factor-alpha - Asahi Type I diabetes vaccine -- Research Corp Typhoid vaccine CVD 908 Kasei, Genetech, Mochida U 143677 -- Pharmacia TNF-Alpha inhibitor -- Tripep TNFR:Fc gene therapy - Targeted Genetics U 81749 -- Pharmacia UA 1248 -- Arizona TNF-SAM2 UGIF -- Sheffield ToleriMab - Innogenetics Toxoplasma gondii vaccine --UIC 2 **UK 101** GlaxoSmithKline UK-279276 – Corvas Intl. TP 9201 -- Telios urodilatin - Pharis TP10 -- Avant TP20 -- Avant uteroferrin-- Pepgen tPA --- Centocor trafermin -- Scios V 20 -- GLYCODesign TRAIL/Apo2L -- Immunex transferrin-binding proteins -- CAMR Transforming growth factor-beta-1 --Genentech transport protein -- Genesis **Pharmaceuticals** TRH -- Ferring Triabin -- Schering AG Triconal Triflavin troponin I -- Boston Life Sciences Systems TRP-2^ -- NIH trypsin inhibitor -- Mochida Peregrine TSP-1 gene therapy -TT-232 vasostatin -- NIH TTS-CD2 -- Active Biotech Tuberculosis vaccine -- Aventis Pasteur, Genesis Tumor Targeted Superantigens -- Active Biotech - Pharmacia tumour vaccines - PhotoCure tumour-activated prodrug antibody Vitaxin conjugates -- Millennium/ImmunoGen tumstatin -- ILEX Tuvirumab -- Novartis WP 652 TV-4710 - Teva

TWEAK receptor -- Immunex

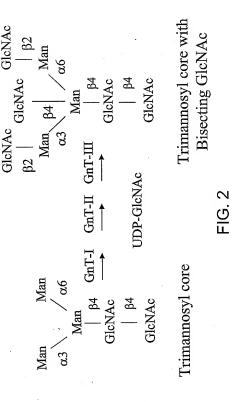
urofollitrophin -- Serono V2 vasopressin receptor gene therapy vaccines -- Active Biotech Varicella zoster glycoprotein vaccine -Research Corporation Technologies Varicella zoster virus vaccine live - Cantab Vascular endothelial growth factor -Genentech, University of California Vascular endothelial growth factors – R&D vascular targeting agents -- Peregrine vasopermeation enhancement agents --VCL -- Bio-Tech, General VEGF - Genentech, Scios VEGF inhibitor -- Chugai VEGF-2 -- Human Genome Sciences VEGF-Trap --- Regeneron viscumin, recombinant -- Madaus Vitrase -- ISTA Pharmaceuticals West Nile virus vaccine -- Bavarian Nordic WT1 vaccine -- Corixa WX-293 -- Wilex BioTech. FIG. 1BB

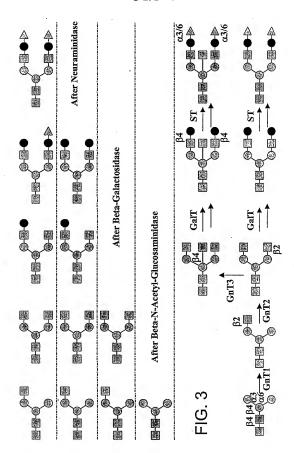
29/345

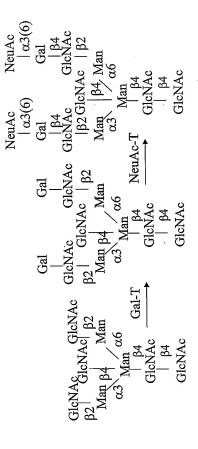
WX-360 -- Wilex BioTech.
WX-UK1 -- Wilex BioTech.
XMP-500 -- XOMA
XomaZyme-791 -- XOMA
XTL 001 -- XTL Biopharmaceuticals
XTL 002 -- XTL Biopharmaceuticals
yeast delivery system -- Globelmmune
Yersinia pestis vaccine
YIGSR-Stealth -- Johnson & Johnson
Yissum Project No. D-0460 -- Yissum

YM 207 – Yamanouchi YM 337 – Protein Design Labs Yttrium-90 labelled biotin Yttrium-90-labelled anti-CEA MAb T84.66 – ZD 0490 – AstraZeneca ziconotide – Elan ZK 157138 – Berlex Laboratories Zollmomab aritox Zorcell – Immune Response

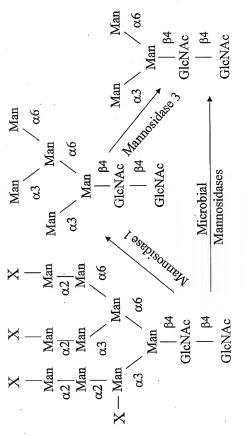
ZRXL peptides -- Novartis



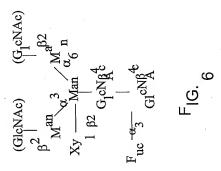


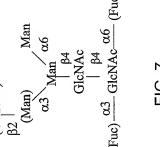


=1G. 4

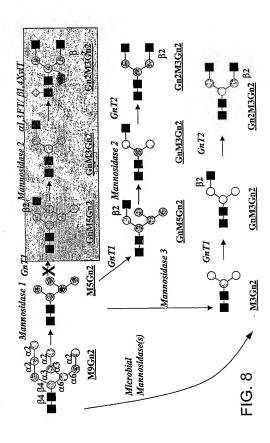


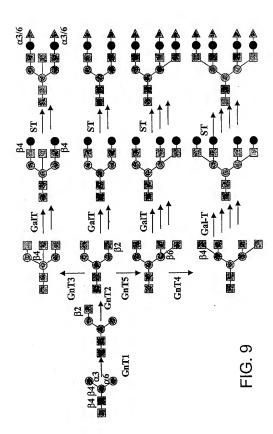
.IG. 5

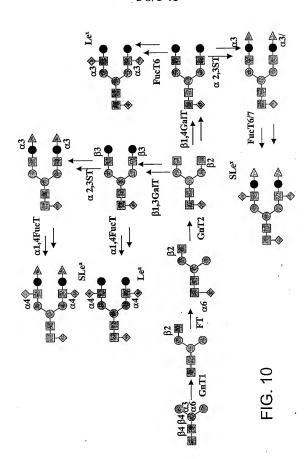




=1G. 7







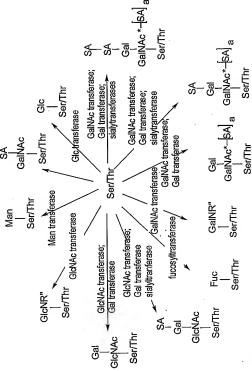


FIG. 11

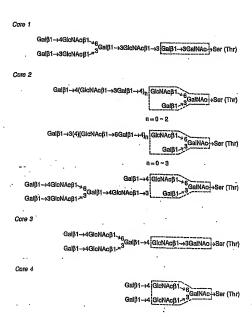
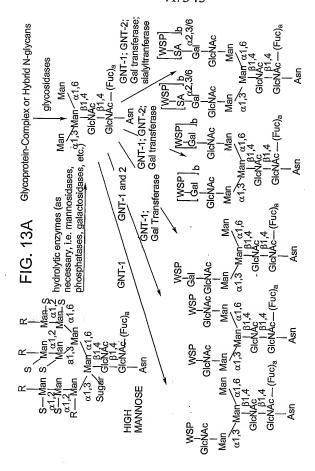
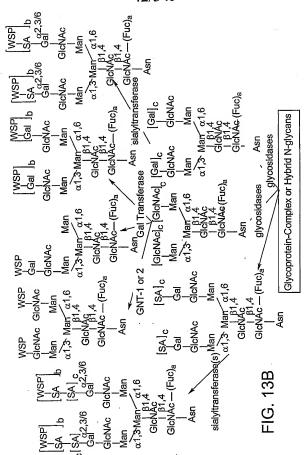


FIG. 12





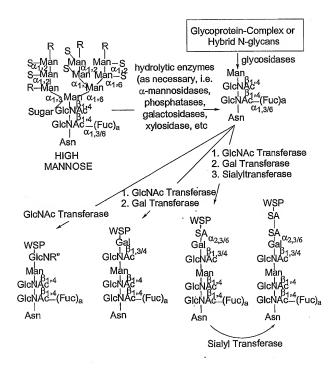


FIG. 14

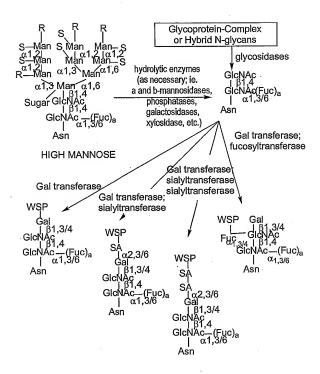


FIG. 15

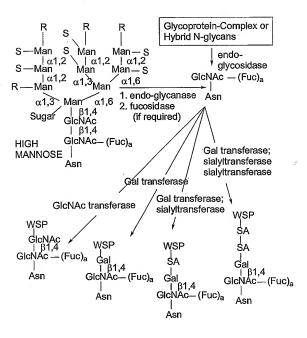
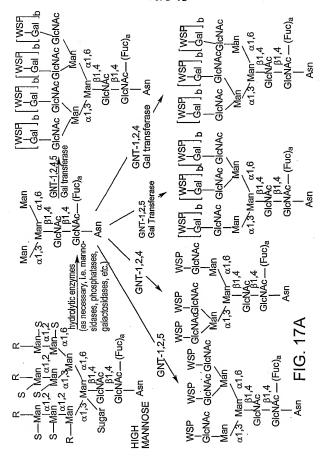
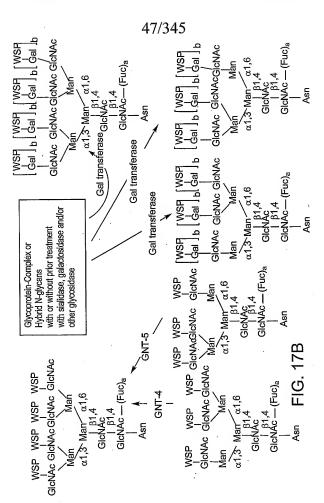
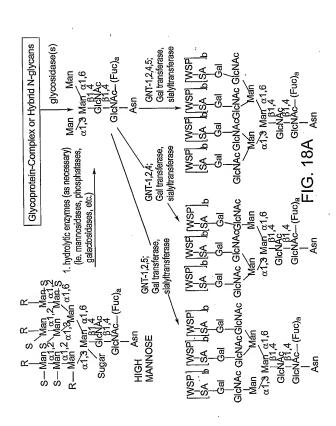
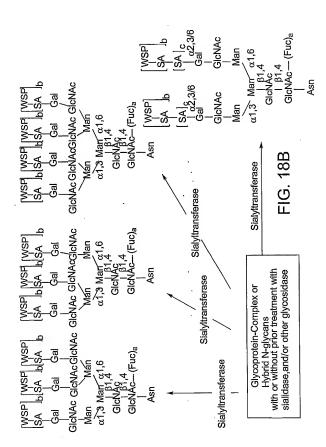


FIG. 16









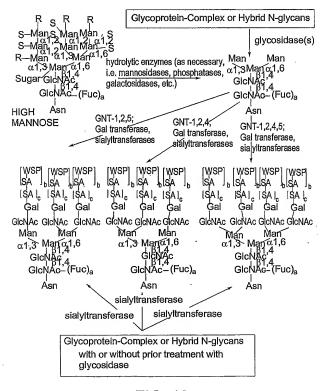
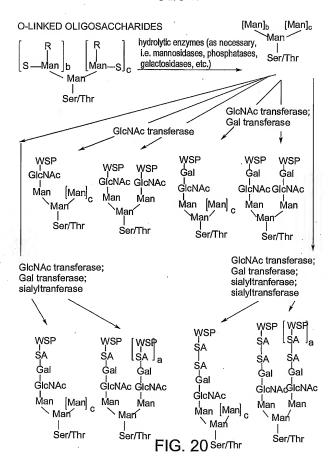
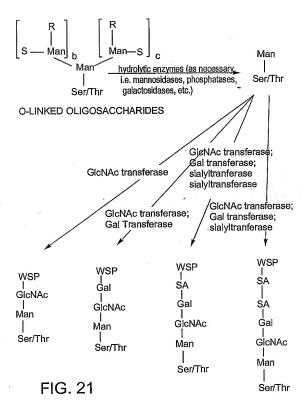


FIG. 19





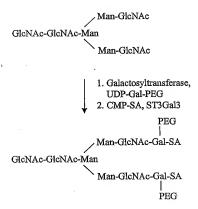


FIG. 22A

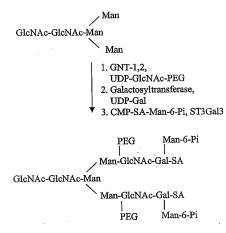


FIG. 22B

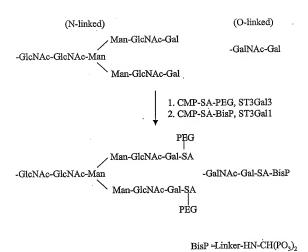
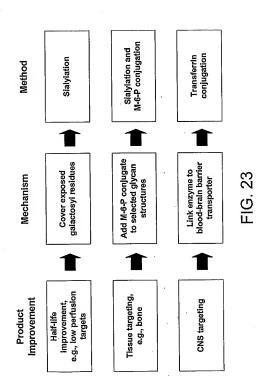


FIG. 22C



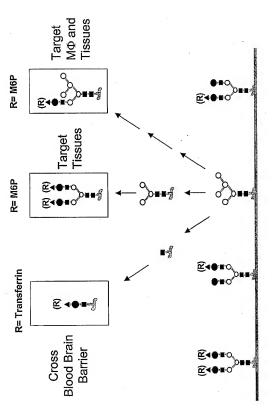
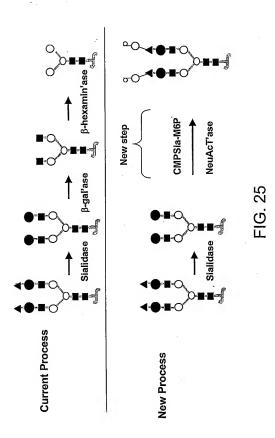


FIG. 24

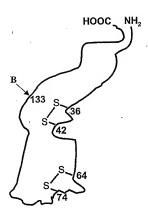




N-acetylglucosamine Mannose Sialic acid Galactose

FIG. 26

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$$\mathbf{B} \leftarrow \begin{pmatrix} (\mathrm{Sia})_b \\ -\mathrm{GalNAc-(Gal)_a-(Sia)_c-(R)_d} \end{pmatrix}_c$$

a-c, e (independently selected) = 0 or 1; d=0; R= modifying group, mannose, oligo-mannose

FIG. 27A

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CHO, BHK, 293 cells, Vero expressed G-CSF a-c, e (independently selected) = 0 or 1; d = 0

Sialidase
 CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 27B

Insect cell expressed G-CSF a, e (independently selected) = 0 or 1; b, c, d = 0.

Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 27C

E. coli expressed G-CSF
a-e = 0.

1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase
c, d, e (independently selected) = 0 or 1;

FIG. 27D

a, b = 0; R = PEG.

NSO expressed G-CSF
a, e (independently selected) = 0 or 1;
b, c, d = 0

1. CMP-SA-levulinate, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; b=0; R = PEG.

2. H₄N₂-PEG

FIG. 27E

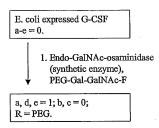


FIG. 27F

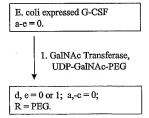


FIG. 27G

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_i \\ -\operatorname{GlcNAe} & (\operatorname{GlcNAc-Man})_{a,l_e^-} & (\operatorname{Sia})_{j_e^-} & (\operatorname{Ria})_{j_e^-} & (\operatorname{Ri$$

$$\mathbf{B} \leftarrow \begin{bmatrix} \text{GlcNAc-Gal})_{cc} - (\text{Sia})_{o} - (R)_{ee} \\ -\text{GalNAc-(Gal)}_{n} - (\text{Sia})_{p} - (R)_{z} \end{bmatrix}_{q}$$

a-d, i, n-u (independently selected) = 0 or 1. aa, bb, cc, dd, ee (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. $v-z=0; \ R=\text{modifying group, mannose, oligo-mannose.} \ R'=H, glycosyl residue, modifying group, glycoconjugate.$

FIG. 28A

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CHO, BHK, 293 cells, Vero expressed interferon alpha 14C.
a-d, aa, bb = 1; e-h = 1 to 4; cc, j-m, i, r-u (independently selected) = 0 or 1; q, n-p, v-z, cc, dd, ee = 0.

Sialidase
 CMP-SA-PEG, ST3Gal3

```
a-d, aa, bb = 1; e-h = 1 to 4;
bb, cc, i, r-u (independently selected) = 0 or 1;
q, n-p, v-z, cc, dd, ee = 0;
v-y (independently selected) = 1,
when j-m (independently selected) = 1;
R = PEG.
```

FIG. 28B

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-q, s, u, v-z, cc, dd, ee = 0; e, g, i, r, t (independently selected) = 0 or 1; aa, bb = 1.
```

1. GNT's 1&2, UDP-GlcNAc 2. Galactosyltransferase, UDP-Gal-PEG

```
b, d, f, h, j-q, s, u, w, y, z, cc, dd, ee = 0;
a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when a, c, (independently selected) = 1;
aa, bb = 1; R = PEG.
```

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Yeast expressed interferon alpha-14C.
a-q, cc, dd, ee, v-z = 0;
r-y (independently selected) = 0 to 1;
aa, bb = 1;
R (branched or linear) = Man, oligomannose or polysaccharide.

- Endo-H
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3
- a-z, bb=0; aa=1; R'=-Gal-Sia-PEG.

FIG. 28D

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$$(Fuc)_{i} \\ A \leftarrow GlcnAc - GlcnAc - Man \\ (R')_{d} \\ (R')_{d} \\ (GlcnAc - Gal)_{a}]_{e} - (Sia)_{j} - (R)_{v} \\ [GlcnAc - (Gal)_{b}]_{r} - (Sia)_{k} - (R)_{w} \\ [GlcnAc - (Gal)_{e}]_{g} - (Sia)_{l} - (R)_{x} \\ [[GlcnAc - (Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y} \\ [[GlcnAc - (Gal)_{d}]_{h} - (R)_{w} \\ [[GlcnAc - (Gal)_{d}]_{h}$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1. R = polymer; R' = sugar, glycoconjugate.

FIG. 28E

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```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.
```

```
1. CMP-SA-PEG, ST3Gal3
```

```
h=1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z=1; n=0; R=PEG.
```

FIG. 28F

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

```
    GNT's 1,2,4,5, UDP-GlcNAc
    Galactosyltransferase, UDP-Gal
    CMP-SA-PEG, ST3Gal3
```

```
a-m, r-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 28G

Yeast expressed interferon alpha-14C. a-n = 0; r-y (independently selected) = 0 to 1; z = 1; R (branched or linear) = Man, oligomannose.

- mannosidases
- 2. GNT's 1,2,4,5, UDP-GlcNAc
- 3. Galactosyltransferase, UDP-Gal
- 4.. CMP-SA-PEG, ST3Gal3

a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.

FIG. 28H

NSO expressed interferon alpha 14C. a-i, r-u (independently selected) = 0 or 1; j-m, n, v-y = 0; z = 1.

> CMP-SA-levulinate, ST3Gal3, buffer, salt
> H₄N₂-PEG

a-i, j-m, r-y (independently selected) = 0 or 1; n = 0; z = 1; R = PEG.

FIG. 281

```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, α2,8-ST

```
h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
z=1; n=0; R=PBG.
```

FIG. 28J

```
CHO, BHK, 293 cells, Vero expressed Interferon alpha-14C.
a-g, j-m, r-u (independently selected) = 0 or 1;
h = 1 to 3; n, v-y = 0; z = 1.
```

- Sialidase
- 2. Trans-sialidase, PEG-Sia-lactose

a-g, j-m, r-y (independently selected) = 0 or 1; h = 1 to 3; n = 0; z = 1; R = PEG.

FIG. 28K

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```
CHO, BHK, 293 cells, Vero expressed interferon alpha-14C.

h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. CMP-SA, α2,8-ST

h = 1 to 3;
a-g, i, r-u (independently selected) = 0 or 1;
j-m (independently selected) = 0 to 40;
z = 1; v-y, n = 0.
```

FIG. 28L

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

```
    GNT's 1 & 2, UDP-GlcNAc
    Galactosyltransferase,
UDP-Gal-linker-SA-CMP
    ST3Gal3, transferrin
```

```
a, c, e, g, i, r, t, v, x (independently selected) = 0 or 1; z=1;\ b,\ d,\ f,\ h,\ j\text{-n},\ s,\ u,\ w,\ y=0; R=transferrin.
```

FIG. 28M

```
Insect cell or fungi expressed interferon alpha-14C. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

- endoglycanase
 - 2. Galactosyltransferase,
 - UDP-Gal-linker-SA-CMP
 - 3. ST3Gal3, transferrin

```
i (independently selected) = 0 or 1;
a-h, j-m, r-z = 0;
n = 1; R' = -Gal-linker-transferrin.
```

FIG. 28N



a-c, e, f (independently selected) = 0 or 1; d, g = 0; R = polymer, glycoconjugate.

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```
CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b).
a-c (independently selected) = 0 or 1; c = 1; d, f, g = 0
```

```
1. Sialidase
2. CMP-SA-PEG, ST3Gal1
```

```
a-d (independently selected) = 0 or 1;
e = 1; b, f, g = 0; R = PEG.
```

FIG. 28P

Insect cell expressed interferon alpha (2a or 2b). a, e (independently selected) = 0 or 1; b, c, d, f, g = 0.

```
    Galactosyltransferase, UDP-Gal
    CMP-SA-PEG, ST3Gal1
```

a, c, d, e (independently selected) = 0 or 1; b, f, g = 0; R = PEG.

FIG. 28Q

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E. coli expressed IF-alpha (2a or 2b). a-g=0.

GalNAc Transferase,
 UDP-GalNAc-PEG

a-c, f, g = 0; d, e = 1; R = PEG.

FIG. 28R

NSO expressed IF-alpha (2a or 2b). a (independently selected) = 0 or 1; e = 1; b, c, d, f, g = 0

1. CMP-SA-levulinate, ST3Gal1 2. H₄N₂-PEG

a, c, d (independently selected) = 0 or 1; e = 1; b, f, g = 0; R = PEG.

FIG. 28S

E. coli expressed IF-alpha (2a or 2b). a-g=0.

 Endo-N-acetylgalatosamidase (synthetic enzyme),
 PEG-Gal-GalNAc-F

a, d, e = 1; b, c, f, g = 0; R = PEG.

FIG. 28T

E. coli expressed IF-alpha (2a or 2b). a-g=0.

GalNAc Transferase, UDP-GalNAc
 sialyltransferase, CMP-SA-PEG

b, d = 0 or 1; e = 1; a, c, f, g = 0; R = PEG.

FIG. 28U

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```
CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b). a-c, f (independently selected) = 0 or 1; e=1;\ d,g=0
```

Sialidase
 CMP-SA-PEG, ST3Gal1 and ST3Gal3

a-d, f, g (independently selected) = 0 or 1; e = 1; R = PEG.

FIG. 28V

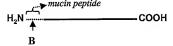
CHO, BHK, 293 cells, Vero expressed IF-alpha (2a or 2b).
a-c, f (independently selected) = 0 or 1; e = 1; d, g = 0

1. Sialidase
2. CMP-SA-linker-SA-CMP,
,ST3Gal1
3. ST3Gal3, transferrin

a-d, f (independently selected) = 0 or 1; e=1; R=transferrin; g=0.

FIG. 28W





a-c, e (independently selected) = 0 or 1; d=0; R = polymer, glycoconjugate.

FIG. 28X

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CHO, BHK, 293 cells, Vero expressed interferon alpha-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d=0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 28Y

Insect cell expressed interferon alpha-mucin fusion protein.

a, e (independently selected) = 0 or 1; b. c. d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 28Z

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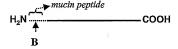
E. coli expressed interferon alpha-mucin fusion protein.

a-e = 0.

- GalNAc Transferase, UDP-GalNAc
 CMP-SA-PEG, sialyltransferase
- c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 28AA





a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 28BB

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E. coli expressed interferon alpha-mucin fusion protein.

a-e, n=0.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 28CC

E. coli expressed interferon alpha-mucin fusion protein.

a-e, n = 0.

GalNAc Transferase,
 UDP-GalNAc-linker-SA-CMP

2. ST3Gal3, asialo-transferrin

3. CMP-SA, ST3Gal3

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

FIG. 28DD

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E. coli expressed Interferon alpha (no fusion). a-e, n=0.

NHS-CO-linker-SA-CMP
 ST3Gal3, transferrin

a-e=0; n=1; R'=linker-transferrin.

FIG. 28EE

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$$\begin{array}{c} (\operatorname{Fuc})_{i} \\ \mathbf{A} \longleftarrow \operatorname{GlcNAc} - \operatorname{GlcNAc} -$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = polymer

FIG. 29A

```
CHO, BHK, 293 cells, Vero expressed IF-beta h=1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z=1.
```

```
    Sialidase
    CMP-SA-PEG, ST3Gal3
```

```
h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 29B

```
Insect cell expressed IF-beta a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0 or 1; z = 1.
```

GNT's 1&2, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal

2. CMP-SA-PEG, ST3Gal3, buffer, salt

```
b, d, f, h, k, m, n, s, u, w, y = 0;
a, c, e, g, i, r, t (independently selected) = 0 or 1;
j, l, v, x (independently selected) = 0 or 1;
z = 1; R = PEG.
```

FIG. 29C

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```
Yeast expressed IF-beta a-n = 0; z = 1; r-y (independently selected) = 0 to 1; R (branched or linear) = Man, oligomannose or polysaccharide.
```

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- 3., CMP-SA-PEG, ST3Gal3

```
a-m, r-z= 0; n = 1; R' = -Gal-Sia-PEG.
```

FIG. 29D

```
h = 1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.

1. CMP-SA-PEG, ST3Gal3

h = 1 to 3;
a-g, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

CHO, BHK, 293 cells, Vero expressed IF-beta

FIG. 29E

$$\label{eq:constraints} \begin{split} & \text{Insect cell expressed IF-beta} \\ & \text{a-d, f, h, j-n, s, u, v-y} = 0; \ e, \ g, \ i, \ r, \ t \\ & \text{(independently selected)} = 0 \ \text{or} \ 1; \ z = 1. \end{split}$$

```
    GNT's 1,2,4,5, UDP-GlcNAc
    Galactosyltransferase, UDP-Gal
    CMP-SA-PEG, ST3Gal3
```

```
a-m, r-y (independently selected) = 0 or 1;
z = 1; n = 0; R = PEG.
```

FIG. 29F

```
Yeast expressed IF-beta

a-n = 0; z = 1;

r-y (independently selected) = 0 to 1;

R (branched or linear) = Man, oligomannose.
```

```
1. mannosidases
2. GNT's 1,2,4,5, UDP-GlcNAc
3. Galactosyltransferase, UDP-Gal
4. CMP-SA-PEG, ST3Gal3
```

```
a-m, r-y (independently selected) = 0 or 1; z = 1; n = 0; R = PEG.
```

```
NSO expressed IF-beta
a-i, r-u (independently selected) = 0 or 1;
j-m, n, v-y = 0; z = 1.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    2. H₄N,-PEG
```

```
a-i, j-m, r-y (independently selected) = 0 or 1;

n = 0; z = 1; R = PEG.
```

FIG. 29H

```
CHO, BHK, 293 cells, Vero expressed IF-beta h=1 to 3;
a-g, j-m, i (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
n, v-y = 0; z = 1.
```

1. CMP-SA-PEG, α2,8-ST

```
\label{eq:heat_section} \begin{split} h &= 1 \text{ to 3;} \\ a - g, i, r - u \text{ (independently selected)} &= 0 \text{ or 1;} \\ j - m \text{ (independently selected)} &= 0 \text{ to 2;} \\ v - y \text{ (independently selected)} &= 1, \\ when j - m \text{ (independently selected)} \text{ is 2;} \\ z &= 1; \ n = 0; \ R = PEG. \end{split}
```

FIG. 291

CHO, BHK, 293 cells, Vero expressed IF-beta a-g, j-m, r-u (independently selected) = 0 or 1; h=1 to 3; n, v-y=0; z=1.

- 1. Sialidase
- 2. Trans-sialidase, PEG-Sia-lactose

a-g, j-m, r-y (independently selected) = 0 or 1; h = 1 to 3; n = 0; z = 1; R = PEG.

FIG. 29J

CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n, v-y=0.

- 1. Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3
- a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n=0;
- v-y (independently selected) = 0 or 1; R = PEG.

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```
NSO expressed Ifn-beta.
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; n, v-y = 0;
Sia (independently selected) = Sia or Gal.
```

1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, r-u, z (independently selected) = 0 or 1;
e-h = 1; R = PEG
n = 0; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
```

FIG. 29L

```
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n, v-y = 0.
```

 Sialidase
 CMP-SA-PEG (16 mol eq), ST3Gal3
 CMP-SA, ST3Gal3

a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h=1; n=0; v-y (independently selected) = 0 or 1; R = PEG.

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CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n, v-y = 0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₂-PEG

a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n = 0; v-y (independently selected) = 0 or 1; R = PEG.

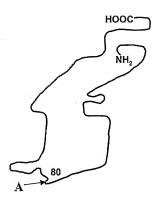
FIG. 29N

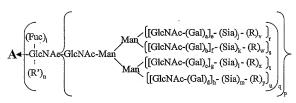
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, r-u, z (independently selected) = 0 or 1; e-h = 1; n, v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, r-u, z (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; n, v-y (independently selected) = 0.

FIG. 290





a-d, i, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group; R' = H, glycosyl group, modifying group, glycoconjugate.

```
\begin{split} &\text{Insect cell expressed Ifn-beta.} \\ &\text{a-d, f, h, j-m, s, u, v-y} = 0; \\ &\text{e, g, i, q, r, } t \text{ (independently selected)} = 0 \text{ or } 1. \end{split}
```

GNT's 1,2,4,5, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal-PEG

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 29Q

```
Yeast expressed Ifn-beta. 
a-m=0; q-y (independently selected) = 0 to 1; p=1; R (branched or linear) = Man, oligomannose.
```

Endoglycanase
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3

```
a-m, p-y=0;
n (independently selected) = 0 or 1;
R'=-Gal-Sia-PEG.
```

FIG. 29R

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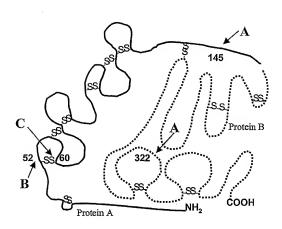
CHO, BHK, 293 cells, Vero expressed Ifn-beta. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

- CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal3, desialylated transferrin.
 - 3. CMP-SA, ST3Gal3

a-m, q-u (independently selected) = 0 or 1; p = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-transferrin.

FIG. 29S

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$$\mathbf{A} \bullet \begin{matrix} (\operatorname{Fuc})_{i} \\ -\operatorname{GlcNAc-GlcNAc-Man} \end{matrix} \begin{matrix} (\operatorname{IGlcNAc-(Gal)}_{a}l_{e}^{-} \cdot (\operatorname{Sia})_{j}^{-} \cdot (R)_{v} \cdot)_{r} \\ (\operatorname{IGlcNAc-(Gal)}_{b}l_{r}^{-} \cdot (\operatorname{Sia})_{k}^{-} \cdot (R)_{w} \cdot)_{s} \\ (\operatorname{IGlcNAc-(Gal)}_{d}l_{g}^{-} \cdot (\operatorname{Sia})_{i}^{-} \cdot (R)_{x} \cdot)_{t} \\ (\operatorname{IGlcNAc-(Gal)}_{d}l_{h}^{-} \cdot (\operatorname{Sia})_{m}^{-} \cdot (R)_{y} \cdot)_{u} \cdot (\operatorname{IGlcNAc-(Gal)}_{d}l_{h}^{-} \cdot (\operatorname{Sia})_{m}^{-} \cdot (R)_{y} \cdot)_{u} \cdot (\operatorname{IGlcNAc-(Gal)}_{d}l_{h}^{-} \cdot (\operatorname{Sia})_{m}^{-} \cdot (R)_{y} \cdot)_{u} \cdot (\operatorname{IGlcNAc-(Gal)}_{d}l_{h}^{-} \cdot (\operatorname{IGlcNAc-(Gal)}_{d}l_$$

$$\mathbf{B} \leftarrow \left(\text{Glc-}(\mathbf{X}\mathbf{y}\mathbf{l})_{n} \right)$$

a-d, i, q-u (independently selected) = 0 or 1. o, p (independently selected) = 0 or 1. e-h, n (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-y = 0; R = modifying group, mannose, oligomannose, Sia-Lewis X. Sia-Lewis A..

FIG. 30A

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BHK expressed Factor VII or VIIa a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, v-y = 0; n = 0-4.

```
    Sialidase
    CMP-SA-PEG (16 mole eq),
ST3Gal3
```

```
a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4; v, x, (independently selected) = 1, when j, l (respectively, independently selected) is 1; R = PEG.
```

FIG. 30B

CHO, BHK, 293 cells, Vero expressed Factor VII or VIIa a-d, e, i, g, q, j, l, o, p (independently selected) = 0 or 1; r, t=1; f, h, k, m, s, u, v-y=0; n=0-4.

```
    Sialidase
    CMP-SA-PEG (1.2 mole eq),
ST3Gal3
    CMP-SA (8 mol eq), ST3Gal3
```

```
a-d, e, g, i, q, j, l, o, p (independently selected) = 0 or 1; r, t = 1; f, h, k, m, s, u, w, y = 0; n = 0-4; v or x, (independently selected) = 1, when j or 1, (respectively, independently selected) is 1; R = PEG.
```

FIG. 30C

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```
NSO expressed Factor VII or VIIa
a--u (independently selected) = 0 or 1;
v-y = 0; n = 0-4;
Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α -galactosidase 2. Galactosyltransferase, UDP-Gal
- I 3. CMP-SA-PEG, ST3Gal3

```
a-m, o-u (independently selected) = 0 or 1;

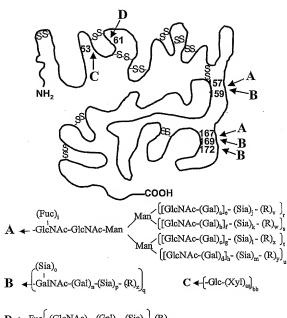
n = 0-4; v-y (independently selected) = 1,

when j-m (independently selected) is 1;

Sia = Sia; R = PEG.
```

FIG. 30D

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D ←-Fuc (GlcNAc)_{cc}-(Gal)_{dd}-(Sia)_{ee} -(R)_{gg}

a-d, i, n-u (independently selected) = 0 or 1. bb, cc, dd, ee, ff, gg (independently selected) = 0 or 1. e-h, aa (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-z = 0: R = modifying group, mannose, oligo-mannose,

FIG. 31A

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q=1; e-h=1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg=0.
```

Sialidase
 CMP-SA-PEG, ST3Gal3

```
a-d, q = 1; e-h = 1 to 4;

aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)

= 0 or 1;

o, p, z = 0;

j-m, ee, v-y, gg (independently selected) = 0 or 1;

R = PEG.
```

FIG. 31B

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

- Sialidase
 - 2. CMP-SA-PEG, ST3Gal3
 - 3. ST3Gal1, CMP-SA

```
a-d, n, p, q = 1; e-h = 1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1;
j-m, ee, v-y, gg (independently selected) = 0 or 1;
o, z = 0; R = PEG.
```

FIG. 31C

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CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q, bb, cc, dd, ff = 1; e-h, aa = 1 to 4; ee, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

- sialidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
- 4. CMP-SA-PEG, ST3Gal1

```
a-d, n, q=1; e-h=1 to 4;
aa, bb, cc, dd, ee, ff, i, r-u (independently selected) = 0 or 1; R=PEG;
o, v-y, gg = 0;
j-m, p, ee (independently selected) = 0 or 1, but when p=1, z=1.
```

FIG. 31D

CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q=1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.

CMP-SA-PEG, ST3Gal3

a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected) = 0 or 1; R = PEG; o, p, z = 0; j-m, ee, v-y, gg (independently selected) = 0 or 1.

FIG. 31E

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```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, q = 1; e-h = 1 to 4; aa, bb, cc, dd, ee, ff, j-m, i, n, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

buffer, salt
2. H₄N₂-PEG

```
a-d, q=1; e-h=1 to 4;
aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)
= 0 or 1;
o, p, z=0; R=PEG;
j-m, ee, v-y, gg (independently selected) = 0 or 1.
```

FIG. 31F

```
CHO, BHK, 293 cells, Vero expressed Factor IX a-d, n, q, bb, cc, dd, ff = 1; e-h, aa = 1 to 4; ee, j-m, i, o, p, r-u (independently selected) = 0 or 1; v-z, gg = 0.
```

1. CMP-SA-PEG, α 2,8-ST

```
a-d, q = 1; e-h = 1 to 4;

aa, bb, cc, dd, ee, ff, i, n, r-u (independently selected)

= 0 or 1;

o, p, z = 0; R= PEG;

j-m, ee (independently selected) = 0 to 2;

v-y, gg (independently selected) = 1, when j-m

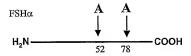
(independently selected) is 2;
```

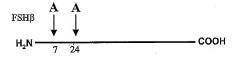
FIG. 31G

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$$\mathbf{A} \leftarrow \underbrace{\left([\operatorname{GlcNAc-(Gal)}_{a}]_{s^{-}} (\operatorname{Sia})_{j} - (R)_{v} \right)_{r}^{T}}_{\left[[\operatorname{GlcNAc-(Gal)}_{b}]_{r} - (\operatorname{Sia})_{k} - (R)_{w} \right]_{s}^{T}}_{\left[[\operatorname{GlcNAc-(Gal)}_{d}]_{b}]_{r} - (\operatorname{Sia})_{k} - (R)_{w} \right]_{s}^{T}}_{\left[[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \right]_{u}} \left(\underbrace{\left[[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \right]_{u}}_{\left[[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \right]_{u}}_{\left[[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \right]_{u}} \left(\underbrace{\left[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \right]_{u}}_{\left[[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \right]_{u}}_{\left[[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \right]_{u}} \left(\underbrace{\left[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \right]_{u}}_{\left[[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (R)_{y} \right]_{u}}_{\left[\operatorname{GlcNAc-(Gal)}_{d}]_{h}} \left(\underbrace{\operatorname{GlcNAc-(Gal)}_{d}}_{\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h}}_{\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h}} \left(\underbrace{\operatorname{GlcNAc-(Gal)}_{d}}_{\left[\operatorname{GlcNAc-(Gal)}_{d} \right]_{h}}_{h} \left(\underbrace{\operatorname{GlcNAc-(Gal)}_{d}}_{h} \right)_{h}}_{h} \right) \right)$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose.

FIG. 32A

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CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1: v-v = 0.

1. Sialidase

2. CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1: v-v (independently selected) = 1, when i-m (independently selected) is 1; R = PEG.

FIG. 32B

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, g-u (independently selected) = 0 or 1; e-h=1: v-v=0.

- Sialidase
- 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3, CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y (independently selected) = 0 or 1; R = PEG.

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NSO expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0; Sia (independently selected) = Sia or Gal.

- Sialidase and α-galactosidase
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal1
- a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = PEG.

FIG. 32D

```
CHO, BHK, 293 cells, Vero expressed FSH.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
```

2. CMP-SA-PEG (16 mol eq), ST3Gal3

3. CMP-SA, ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 32E

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H,N,-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 32F

CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 32G

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```
Insect cell expressed FSH.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
    GNT's 1,2,4,5, UDP-GlcNAc
    Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1;
j-m=0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R=PEG.
```

FIG. 32H

```
Yeast expressed FSH.

a-m=0; q-y (independently selected) = 0 to 1;

p=1;

R (branched or linear) = Man, oligomannose.
```

- Endoglycanase
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3
- a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

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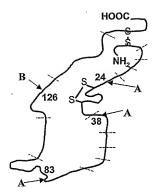
CHO, BHK, 293 cells, Vero expressed FSH. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

 CMP-SA-linker-SA-CMP, ST3Gal3
 ST3Gal1, desialylated chorionic gonadrophin (CG) produced in CHO.
 CMP-SA, ST3Gal3, ST3Gal1

a-m, q-u (independently selected) = 0 or 1; p = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-CG.

FIG. 32J

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$$\begin{array}{c} (\operatorname{Fuc})_{i} \\ \mathbf{A} \leftarrow -\operatorname{GlcNAc-GlcNAc-Man} \\ & \left[(\operatorname{GlcNAc-(Gal)}_{\mathfrak{g}}|_{\mathfrak{g}^{-}} (\operatorname{Sia})_{\mathfrak{f}^{-}} (\operatorname{R})_{\mathfrak{g}} \right]_{\mathfrak{g}} \\ & \left[(\operatorname{GlcNAc-(Gal)}_{\mathfrak{g}}|_{\mathfrak{g}^{-}} (\operatorname{Sia})_{\mathfrak{f}^{-}} (\operatorname{R})_{\mathfrak{g}} \right]_{\mathfrak{g}} \\ & \left[(\operatorname{GlcNAc-(Gal)}_{\mathfrak{g}}|_{\mathfrak{g}^{-}} (\operatorname{Sia})_{\mathfrak{f}^{-}} (\operatorname{R})_{\mathfrak{g}} \right]_{\mathfrak{g}} \\ & \left[(\operatorname{GlcNAc-(Gal)}_{\mathfrak{g}}|_{\mathfrak{g}^{-}} (\operatorname{Sia})_{\mathfrak{g}^{-}} (\operatorname{R})_{\mathfrak{g}} \right]_{\mathfrak{g}} \\ & \left[(\operatorname{GlcNAc-(Gal)}_{\mathfrak{g}}|_{\mathfrak{g}^{-}} (\operatorname{Sia})_{\mathfrak{g}^{-}} (\operatorname{R})_{\mathfrak{g}} \right]_{\mathfrak{g}} \\ & \left[(\operatorname{GlcNAc-(Gal)}_{\mathfrak{g}}|_{\mathfrak{g}^{-}} (\operatorname{Sia})_{\mathfrak{g}^{-}} (\operatorname{R})_{\mathfrak{g}} \right]_{\mathfrak{g}} \\ & \left[(\operatorname{GlcNAc-(Gal)}_{\mathfrak{g}^{-}} (\operatorname{Sia})_{\mathfrak{g}^{-}} (\operatorname{R})_{\mathfrak{g}^{-}} (\operatorname{R})_{\mathfrak{g}} \right]_{\mathfrak{g}} \\ & \left[(\operatorname{GlcNAc-(Gal)}_{\mathfrak{g}^{-}} (\operatorname{Sia})_{\mathfrak{g}^{-}} (\operatorname{R})_{\mathfrak{g}^{-}} (\operatorname{R})_$$

a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. v-z=0; R=modifying group, mannose, oligo-mannose.

FIG. 33A

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```
CHO, BHK, 293 cells, Vero expressed EPO a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; v-z=0
```

Sialidase
 CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

FIG. 33B

```
Insect cell expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.
```

- GNT's 1&2, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3
- b, d, f, h, k, m-q, s, u, w, y, z=0; a, c, e, g, i, r, t (independently selected)= 0 or 1; j, l, v, x (independently selected) = 0 or 1; R=PEG.

FIG. 33C

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```
CHO, BHK, 293 cells, Vero expressed EPO a-q, r-u (independently selected) = 0 or 1; v-z = 0.
```

- 1. sialidase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA, ST3Gal3
- ↓ 4. CMP-SA-PEG, ST3Gal1

```
a-h, n, q = 1;
i-m, o, r-u (independently selected) = 0 or 1;
v-y = 0; p, z = 0 or 1; R = PEG.
```

FIG. 33D

```
CHO, BHK, 293 cells, Vero expressed EPO
a-g, n, q = 1; h = 1 to 3;
j-m, i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 or 1;
v-z = 0
```

1. CMP-SA-PEG, ST3Gal3

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m, v-y (independently selected) = 0 or 1;
R = PEG; z = 0.
```

FIG. 33E

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Insect cell expressed EPO a-d, f, h, j-m, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

GNT's 1, 2 & 5, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal-PEG

a-c, e-g, n, q-t, v-x, z (independently selected) = 0 or 1; d, h, j-m, o, p, y, z = 0; R = PEG.

FIG. 33F

Insect cell expressed EPO a-d, f, h, j-q, s, u, v-z = 0; e, g, i, r, t (independently selected) = 0 or 1.

- 1. GNT's 1, 2 & 5, UDP-GlcNAc
- Galactosidase (synthetic enzyme), PEG-Gal-F.

a-c, e-g, n, q-t, v-x, z (independently selected) = 0 or 1; d, h, j-m, o, p, y, z = 0; R = PEG.

FIG. 33G

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```
NSO expressed NESP q = 1; a-i, n, r-u (independently selected) = 0 or 1; j-m, o, p, v-z = 0
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>a</sub>N<sub>7</sub>-PEG
```

```
q = 1; a-i, j-n, r-y (independently selected) = 0 or 1;
o, p, z = 0; R = PEG.
```

FIG. 33H

```
CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 or 1; v-z = 0
```

1. CMP-SA-PEG, α2,8-ST

```
a-g, n, q = 1; h = 1 to 3;
i, o, p (independently selected) = 0 or 1;
r-u (independently selected) = 0 to 1;
j-m (independently selected) = 0 to 2;
v-y (independently selected) = 1,
when j-m (independently selected) is 2;
R = PEG; z = 0.
```

FIG. 331

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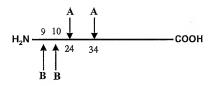
CHO, BHK, 293 cells, Vero expressed NESP a-g, n, q = 1; h = 1 to 3; j-m, i, o, p (independently selected) = 0 or 1; r-u (independently selected) = 0 to1; v-z = 0

1. CMP-SA, poly-α2,8-ST

a-g, n, q = 1; h = 1 to 3; i, j-m, o, p, r-u, (independently selected) = 0 or 1; v-z (independently selected) = 0-40; R = Sia.

FIG. 33J

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$$\begin{array}{c} \boldsymbol{A} & \longleftarrow \begin{pmatrix} [\operatorname{GlcNAc-(Gal)}_{s}]_{e^{-}} (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \\ [\operatorname{GlcNAc-GlcNAc-Man} \\ & \longrightarrow \begin{pmatrix} [\operatorname{GlcNAc-(Gal)}_{s}]_{e^{-}} (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \\ [\operatorname{GlcNAc-(Gal)}_{o}]_{g} - (\operatorname{Sia})_{l} - (\operatorname{R})_{x} \\ [\operatorname{GlcNAc-(Gal)}_{o}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \\ \end{pmatrix}_{l} \\ & \longrightarrow \begin{pmatrix} [\operatorname{GlcNAc-(Gal)}_{o}]_{e^{-}} (\operatorname{Sia})_{l} - (\operatorname{R})_{v} \\ [\operatorname{GlcNAc-(Gal)}_{o}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \\ \end{bmatrix}_{l} \\ & \longrightarrow \begin{pmatrix} [\operatorname{GlcNAc-(Gal)}_{o}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (\operatorname{R})_{y} \\ (\operatorname{GlcNAc-(Gal)}_{o}]_{h^{-}} (\operatorname{GlcNAc-(Gal)}_{o})_{m^{-}} (\operatorname{ClcNAc-(Gal)}_{o})_{m^{-}} (\operatorname{ClcNAc-(Gal)}_{o})_{m^{-}}$$

$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{\mathrm{o}} \\ -\mathrm{GaINAc-(GaI)_{n}-(Sia)_{p}-(R)_{z}} \end{bmatrix}_{\mathrm{aa}}$$

a-d, i, n-u, as (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 34A

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```
CHO, BHK, 293 cells, Vero expressed GM-CSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq),
```

ST3Gal3

```
a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 34B

```
CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z=0.
```

```
1. Sialidase
2. CMP-SA-PEG (1.2 mol eq),
ST3Gal3

▼ 3. CMP-SA (16 mol eq), ST3Gal3 &
ST3Gal1
```

```
a-d, i-m, p-u, aa (independently selected) = 0 or 1;
o, z = 0; n, e-h = 1;
v-y (independently selected) = 0 or 1; R = PEG.
```

FIG. 34C

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```
NSO expressed GM-CSF.
a-d, i-m, o-u, aa (independently selected) = 0 or 1;
n, e-h = 1; v-z = 0;
Sia (independently selected) = Sia or Gal.
```

- 1. Sialidase and α-galactosidase
- CMP-SA, ST3Gal3
- CMP-SA-PEG, ST3Gal1

```
a-d, i-m, p-u, z, as (independently selected) = 0 or 1; n, e-h = 1; o, v-y = 0; z = 1, when p = 1; R = PEG.
```

FIG. 34D

```
CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.
```

- 1. Sialidase
- CMP-SA-PEG (16 mol eq), ST3Gal3
 - 3. CMP-SA, ST3Gal3

a-d, i-m, q-y, as (independently selected) = 0 or 1; o, p, z = 0; n, e-h = 1; R = PEG.

FIG. 34E

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CHO, BHK, 293 cells, Vero expressed GM-CSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h=1; v-z=0.

 CMP-SA-levulinate, ST3Gal3, buffer, salt
 H₄N₇-PEG

a-d, i-m, o-y, aa (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = PEG.

FIG. 34F

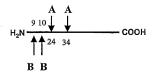
CHO, BHK, 293 cells, Vero expressed GMCSF. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z=0.

1. CMP-SA, α2,8-ST

a-d, i, o-u, as (independently selected) = 0 or 1; n, e-h = 1; j-m (independently selected) = 0-20; v-z (independently selected) = 0.

FIG. 34G

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$$\mathbf{A} \overset{[[GlcNAc-(Gal)_a]_c^- (Sia)_j^- (R)_v]_r}{[[GlcNAc-(Gal)_b]_r^- (Sia)_k^- (R)_w]_s} \\ \mathbf{A} \overset{[[GlcNAc-(Gal)_b]_r^- (Sia)_k^- (R)_w]_s}{[[GlcNAc-(Gal)_c]_g^- (Sia)_l^- (R)_x]_t} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_d]_r^- (Sia)_m^- (R)_y]_u}{[[GlcNAc-(Gal)_d]_h^- (Sia)_m^- (R)_y]_u} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_b]_r^- (Sia)_m^- (R)_y]_u}{[[GlcNAc-(Gal)_d]_h^- (Sia)_m^- (R)_y]_u} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_b]_r^- (Sia)_k^- (R)_w]_s}{[[GlcNAc-(Gal)_d]_h^- (Sia)_m^- (R)_y]_u} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_b]_r^- (Sia)_k^- (R)_w]_s}{[[GlcNAc-(Gal)_d]_h^- (Sia)_m^- (R)_w]_u} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_b]_r^- (Sia)_h^- (R)_w]_s}{[[GlcNAc-(Gal)_d]_h^- (Sia)_m^- (R)_w]_u} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_b]_r^- (Sia)_h^- (R)_w]_s}{[[GlcNAc-(Gal)_d]_h^- (Sia)_m^- (R)_w]_u} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_b]_r^- (Sia)_h^- (R)_w]_u}{[[GlcNAc-(Gal)_d]_h^- (Sia)_m^- (R)_w]_u} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_b]_r^- (Sia)_h^- (R)_w]_u}{[[GlcNAc-(Gal)_d]_h^- (Sia)_m^- (R)_w]_u} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_h]_h^- (Sia)_h^- (R)_w]_u}{[[GlcNAc-(Gal)_h]_h^- (R)_w]_u} \\ \mathbf{Man} \overset{[[GlcNAc-(Gal)_h]_h^- (R)_w}{[[GlcNAc-(Gal)_h]_h^- (R)_w} \\ \mathbf{M$$

$$\mathbf{B} \leftarrow \begin{bmatrix} (\operatorname{Sia})_{0} \\ -\operatorname{GalNAc-(Gal)}_{n} - (\operatorname{Sia})_{p} - (R)_{z} \end{bmatrix}_{aa}$$

a-d, i, n-u, aa, bb, cc (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose. R'= H, glycosyl residue, modifying group. glycoconjugate.

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```
Insect cell expressed GM-CSF.
a-d, f, h, j-m, o, p, s, u, v-z = 0;
e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

```
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, n, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 341

```
Yeast expressed GM-CSF.
a-p, z, &c = 0;
q-y, aa (independently selected) = 0 to 1;
bb = 1; R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

- 1. Endoglycanase
- 2. mannosidase (if aa = 1).
- 3. Galactosyltransferase, UDP-Gal-PEG

```
a-p, r-z, aa, bb = 0;
q, cc (independently selected) = 0 or 1;
R' = -Gal-PEG.
```

FIG. 34J

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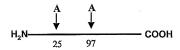
CHO, BHK, 293 cells, Vero expressed GM-CSF. a--m, o-u, aa, bb (independently selected) = 0 or 1; n, v-z, cc = 0.

- 1. sialidase
- CMP-SA, ST3Gal3
 CMP-SA-linker-SA-CMP, ST3Gal1
 ST3Gal3, transferrin

a--m, p-u, z, aa (independently selected) = 0 or 1; o, v-y, cc = 0; bb, n = 1; R = transferrin.

FIG. 34K

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & \operatorname{Man} \left([\operatorname{GlcNAc-(Gal)}_{a}]_{s^{-}} (\operatorname{Sia})_{j} - (R)_{v} \right)_{r} \\ (\operatorname{GlcNAc-GlcNAc-Man} & \left([\operatorname{GlcNAc-(Gal)}_{b}]_{s^{-}} (\operatorname{Sia})_{k} - (R)_{w} \right)_{s} \\ (\operatorname{GlcNAc-(Gal)}_{a}]_{g^{-}} (\operatorname{Sia})_{i} - (R)_{x} \right)_{t} \\ (\operatorname{[GlcNAc-(Gal)}_{a}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (R)_{y})_{u} \\ (\operatorname{GlcNAc-(Gal)}_{a}]_{h^{-}} (\operatorname{Sia})_{m^{-}} (R)_{y} \end{bmatrix}_{t}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 35A

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```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 35B

```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-PEG (1.2 mol eq),
ST3Gal3
    CMP-SA (16 mol eq), ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.
```

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```
NSO expressed Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.
```

```
    Sialidase and α-galactosidase
    α-Galactosyltransferase, UDP-Gal
    3. CMP-SA-PEG, ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 35D

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
    CMP-SA, ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 35E

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```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-levulinate, ST3Gal3,
2. H<sub>4</sub>N<sub>2</sub>-PEG

a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 35F

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST
```

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

FIG. 35G

PCT/US02/32263

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$$\mathbf{A} \bullet \begin{bmatrix} (\operatorname{Fuc})_i \\ - (\operatorname{GlcNAc-(Gal)_a}]_e - (\operatorname{Sia})_j - (\operatorname{R})_v \end{bmatrix}_r \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_b}]_f - (\operatorname{Sia})_k - (\operatorname{R})_w \end{bmatrix}_e \\ (\operatorname{R}')_n \\ \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_g - (\operatorname{Sia})_l - (\operatorname{R})_x \end{bmatrix}_t \\ \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} (\operatorname{GlcNAc-(Gal)_a}]_h - (\operatorname{Gal)_a}]_h - (\operatorname{Gal)_a}_h - (\operatorname{Gal)_a}_h$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 35H

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```
Insect or fungi cell expressed IF-gamma.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 351

```
Yeast expressed IF-gamma. 
a-m=0; q-y (independently selected) = 0 to 1; p=1; R (branched or linear) = Man, oligomannose.
```

- Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

FIG. 35J

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```
CHO, BHK, 293 cells, Vero expressed IF-gamma. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

CMP-SA-linker-Gal-UDP, ST3Gal3
 Galactosyltransferase, transferrin treated with endoglycanase.

```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 35K

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h, p = 1; n, v-y = 0.

1. CMP-SA-PEG,
ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1; e-h, p=1; n, v-y (independently selected) = 0 or 1; R=PEG.
```

FIG. 35L

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```
Insect or fungi cell expressed IF-gamma.

a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.

1. GNT's 1 & 2, UDP-GlcNAc-PEG

a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, q (independently selected) = 0 or 1;
p = 1; v, x (independently selected) = 1,
when e, g (independently selected) is 1;
R = PEG.
```

FIG. 35M

```
CHO, BHK, 293 cells, Vero expressed
Interferon gamma.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. CMP-SA-PEG, α2,8-ST
```

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-2;
v-y (independently selected) = 1,
when j-m (independently selected) = 2;
R = PEG.
```

FIG. 35N

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$$\mathbf{A} \leftarrow \underbrace{\left([\mathrm{GlcNAc} - (\mathrm{Gal})_{a}]_{s} - (\mathrm{Sia})_{j} - (\mathrm{R})_{v} \right)_{r}}_{\left[[\mathrm{GlcNAc} - (\mathrm{Gal})_{b}]_{s} - (\mathrm{Sia})_{t} - (\mathrm{R})_{w} \right]_{s}}_{\left[[\mathrm{GlcNAc} - (\mathrm{Gal})_{d}]_{s} - (\mathrm{Sia})_{t} - (\mathrm{R})_{x} \right]_{t}}_{\left[[\mathrm{GlcNAc} - (\mathrm{Gal})_{d}]_{h} - (\mathrm{Sia})_{m} - (\mathrm{R})_{y} \right]_{u}} \left([\mathrm{GlcNAc} - (\mathrm{Gal})_{d}]_{h} - (\mathrm{Sia})_{m} - (\mathrm{R})_{y} \right)_{u}} \left([\mathrm{GlcNAc} - (\mathrm{Gal})_{d}]_{h} - (\mathrm{Sia})_{m} - (\mathrm{R})_{y} \right)_{u}} \right)_{u} \left([\mathrm{GlcNAc} - (\mathrm{Gal})_{d}]_{h} - (\mathrm{Sia})_{m} - (\mathrm{R})_{y} \right)_{u}} \right)$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

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CHO, BHK, 293 cells, Vero or transgenic animal expressed α_1 antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
```

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = PEG.

FIG. 36B

CHO, BHK, 293 cells, Vero or transgenic animal expressed α_1 antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

- 1. Sialidase 2. CMP-SA-PEG (1.2 mol eq), ST3Gal3
- 3. CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R=PEG.

FIG. 36C

131/345

```
NSO expressed \alpha_1-antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.
```

```
1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal
3. CMP-SA-PEG, ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 36D

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed alpha-1 antitrypsin.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
    CMP-SA, ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 36E

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CHO, BHK, 293 cells, Vero or transgenic animal expressed α_1 -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA-levulinate, ST3Gal3, buffer, salt 2. H₄N₅-PEG

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

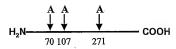
FIG. 36F

CHO, BHK, 293 cells, Vero expressed α_1 -antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-v = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

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$$\mathbf{A} = \underbrace{\left([\operatorname{GlcNAc-(Gal)}_{a}]_{a^{-}} (\operatorname{Sia})_{j^{-}} (R)_{v} \right)_{r}}_{\left([\operatorname{GlcNAc-(Gal)}_{b}]_{a^{-}} (\operatorname{Sia})_{j^{-}} (R)_{w} \right)_{s}}_{\left([\operatorname{GlcNAc-(Gal)}_{d}]_{b^{-}} (\operatorname{Sia})_{l^{-}} (R)_{x} \right)_{t}}_{\left([\operatorname{GlcNAc-(Gal)}_{d}]_{b^{-}} (\operatorname{Sia})_{m^{-}} (R)_{y} \right)_{u} \in \mathbb{R}^{d}}$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. y-y=0; R = modifying group, mannose, oligo-mannose;

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 36H

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Insect or fungi cell expressed α_1 -antitrypsin. a-d, f, h, j-m, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1.

```
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1; j-m = 0; v-y (independently selected) = 1, when e-h (independently selected) is 1; R = PEG.
```

FIG. 361

 $\begin{array}{l} \mbox{Yeast expressed} \ \, \alpha_1\mbox{-antitrypsin.} \\ \mbox{a-m} = 0; \ \, q\mbox{-y} \ \, (\mbox{independently selected}) = 0 \ \, \mbox{to} \ \, 1; \\ \mbox{p} = 1; \ \, R \ \, (\mbox{branched or linear}) = \mbox{Man, oligomannose.} \end{array}$

- 1. Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-m, p-y=0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

FIG. 36J

135/345

```
CHO, BHK, 293 cells, Vero expressed \alpha_1-antitrypsin. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

- CMP-SA-linker-Gal-UDP, ST3Gal3
- 2. Galactosyltransferase, transferrin treated with endoglycanase

```
a-m, q-u (independently selected) = 0 or 1;

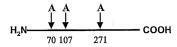
p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker-transferrin.
```

FIG. 36K

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$$\begin{array}{c} \text{(Fuc)}_{i} \\ \textbf{A} \leftarrow \text{-GlcNAc-GlcNAc-Man} \\ \text{(R')}_{p} \\ \end{array} \\ \begin{array}{c} \text{Man} \\ \begin{bmatrix} [\text{GlcNAc-(Gal)}_{b}]_{e^{-}} (\text{Sia})_{i}^{-} (\text{R})_{w} \\ \\ [[\text{GlcNAc-(Gal)}_{c}]_{g^{-}} (\text{Sia})_{e^{-}} (\text{R})_{x} \\ \\ \\ [[\text{GlcNAc-(Gal)}_{d}]_{e^{-}} (\text{Sia})_{m^{-}} (\text{R})_{y} \\ \\ \end{bmatrix}_{y} \\ \\ n \\ \end{array}$$

a-d, i, n-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 to 20.

R = polymer;

R', R" (independently selected) = sugar, glycoconjugate.

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Yeast expressed alpha-1 antitrypsin. a-h, i-m, p, q = 0; R (independently selected) = mannose, oligomannose, polymannose; r-u, v-y (independently selected) = 0 or 1; n, o = 1.

- 1. endoglycanase
- ▼ 2. Galactosyltransferase, UDP-Gal-PEG

```
a-h, i-o, q, r-u, v-y = 0; p = 1.
R" = Gal-PEG.
```

FIG. 36M

Plant expressed alpha-1 antitrypsin. a-d, f, h, j-m, s, u , v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1; n=1; R'=xylose

- 1. hexosaminidase,
- 2. alpha mannosidase and xylosidase
- 3. GlcNAc transferase, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, v-y = 0;
e, g, i, r, t (independently selected) = 0;
q = 1; R' = GlcNAc-PEG.
```

FIG. 36N

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CHO, BHK, 293 cells, Vero, transgenic animal expressed α_1 antitrypsin. a-h, i-o, r-u (independently selected) = 0 or 1; p, q, v-y = 0.

 CMP-SA-PEG, ST3Gal3

a-h, i-o, r-u (independently selected) = 0 or 1; p, q = 0; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 360

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$$\begin{array}{c} \text{(Fuc)}_{i} \\ \text{(Fuc)}_{i} \\ \text{(GlcNAc-(Gal)}_{a}]_{e}^{-} \text{(Sia)}_{j}^{-} \text{(R)}_{v} \\ \text{([GlcNAc-(Gal)}_{b}]_{r}^{-} \text{(Sia)}_{k}^{-} \text{(R)}_{w} \\ \text{([GlcNAc-(Gal)}_{a}]}_{g}^{-} \text{(Sia)}_{l}^{-} \text{(R)}_{x} \\ \text{([GlcNAc-(Gal)}_{d}]_{h}^{-} \text{(Sia)}_{m}^{-} \text{(R)}_{y} \\ \text{([GlcNAc-(Gal)}_{d}]_{h}^{-} \text{(Sia)}_{m}^{-} \text{(R)}_{y} \\ \text{([GlcNAc-(Gal)}_{d}]_{h}^{-} \text{(Sia)}_{m}^{-} \text{(R)}_{y} \\ \text{([GlcNAc-(Gal)}_{d}]_{h}^{-} \text{(Sia)}_{m}^{-} \text{(R)}_{y} \\ \text{(Sia)}_{m}^{-} \text{(R)}_{y} \\ \text{([GlcNAc-(Gal)}_{d}]_{h}^{-} \text{(Sia)}_{m}^{-} \text{(R)}_{y} \\ \text{(R)}_{m}^{-} \text{(R)}_{m}^{-} \text{(R)}_{m}^{-} \text{(R)}_{m}^{-} \\ \text{(R)}_{m}^{$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

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```
CHO, BHK, 293 cells, Vero expressed Cerezyme a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 37B

```
CHO, BHK, 293 cells, Vero expressed Cerezyme.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-M-6-P (1.2 mol eq),
ST3Gal3
    CMP-SA (16 mol eq), ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = mannose-6-phosphate
```

FIG. 37C

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```
NSO expressed Cerezyme.

a-d, i-m, q-u (independently selected) = 0 or 1;

e-h = 1; v-y = 0;

Sia (independently selected) = Sia or Gal.
```

1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = mannose-6 phosphate
```

FIG. 37D

```
CHO, BHK, 293 cells, Vero expressed Cerezyme.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0.

1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
3. CMP-SA, ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = Mannose-6-phosphate
```

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CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>4</sub>N<sub>4</sub>-spacer-M-6-P or clustered M-6-P
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = M-6-P or clustered M-6-P
```

FIG. 37F

```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
1. CMP-SA, α2,8-ST
```

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1; j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

FIG. 37G

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a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

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```
Insect cell expressed Cerezyme.
a-d, f, h, j-m, s, u, v-y = 0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 371

```
Yeast expressed Cerezyme. 
a-m = 0; q-y (independently selected) = 0 to 1; 
p = 1; R (branched or linear) = Man, oligomannose.
```

- Endoglycanase
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-PEG, ST3Gal3

```
a-m, p-y = 0; n (independently selected) = 0 or 1;
R' = -Gal-Sia-PEG.
```

FIG. 37J

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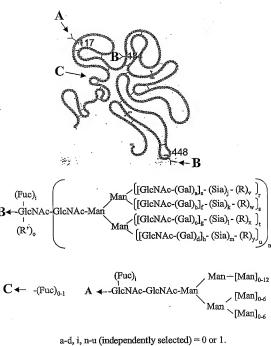
```
CHO, BHK, 293 cells, Vero expressed Cerezyme. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
1. CMP-SA-linker-SA-CMP,
ST3Gal3
2. ST3Gal3, desialylated transferrin.
3. CMP-SA, ST3Gal3
```

```
a-m, q-u (independently selected) = 0 or 1; 
 p = 1; n = 0; v-y (independently selected) = 0 or 1; 
 R = linker-transferrin.
```

FIG. 37K

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a-d, i, n-u (independently selected) = 0 or 1 e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

FIG. 38A

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```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n=1; h=1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; o, v-y = 0.
```

Mannosidase(s), sialidase
 GNT1,2 (4 and/or 5) UDP-GlcNAc
 Gal transferase, UDP-Gal
 CMP-SA-PEG, ST3Gal3

```
A = B; a-g, n = 1; h = 1 to 3;
i, r-u (independently selected) = 0 or 1;
o = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG
```

FIG. 38B

```
Insect or fungi cell expressed tPA A=B;\ a\text{-d},\ f,\ h,\ j\text{-o},\ s,\ u,\ v\text{-y}=0; e, g, i, n, r, t (independently selected) = 0 or 1.
```

1. GNT's 1&2, UDP-GlcNAc 2. Galactosyltransferase, UDP-Gal 3. CMP-SA-PEG, ST3Gal3

```
A=B; \ b,d,\ f,\ h,\ k,m,o,s,u,w,y=0; a, c, e, g, i, r, t (independently selected) = 0 or 1; n=1; j,l,v,x (independently selected) = 0 or 1; R=PEG.
```

FIG. 38C

Yeast expressed tPA B = A; i = 0.

- endoglycanase
 Galactosyltrans
- Galactosyltransferase,
 UDP-Gal-PEG

A = B; a-n, r-y = 0; o = 1; R' = Gal-PEG.

FIG. 38D

Insect or fungi cell expressed tPA

A = B; a-d, f, h, j-o, s, u, v-y = 0;

e, g, i, n, r, t (independently selected) = 0 or 1.

- 1, alpha and beta mannosidases
- 2. Galactosyltransferase, UDP-Gal-PEG

A = B; a-n, r-y = 0; o = 1; R' = Gal-PEG.

FIG. 38E

Insect or fungi cell expressed tPA $A=B;\ a-d,\ f,\ h,\ j-o,\ s,\ u,\ v-y=0;$ e, g, i, n, r, t (independently selected) = 0 or 1.

- 1. GNT's 1&2, UDP-GlcNAc
- 2. Galactosyltransferase, UDP-Gal-PEG

A=B; b, d, f, h, j-o, s, u, w, y=0; a, c, e, g, i, r, t, v, x (independently selected)=0 or 1; n=1; R=PEG.

FIG. 38F

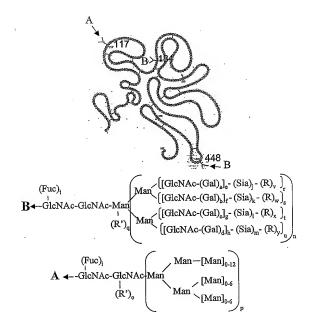
Insect or fungi cell expressed tPA A=B; a-d, f, h, j-o, s, u, v-y = 0; e, g, i, n, r, t (independently selected) = 0 or 1.

- 1. GNT's 1 & 2, UDP-GlcNAc
- Galactosidase (synthetic enzyme), PEG-Gal-F.

 $\begin{array}{lll} A=B; & b,d, \ f, \ h, \ j\text{-o}, s,u,w,y=0;\\ a,c,e,g, \ i, \ r, \ t,v,x \ (independently \ selected)=0 \ or \ 1;\\ n=1; \ R=PEG. \end{array}$

FIG. 38G

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a-d, i, n-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 to 20. R = polymer; R' = sugar, glycoconjugate.

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```
NSO expressed tPA
A = B; a-m, r-u (independently selected) = 0 or 1;
n = 1; o, p, q, v-y = 0
```

```
1. sialidase, alpha-galactosidase
2. CMP-SA-levulinate, ST3Gal3,
3. U.N. PEG.
```

```
A = B; a-m, r-y (independently selected) = 0 or 1;

n = 1; o, p, q = 0;

v-y (independently selected) = 1,

when j-m (independently selected) is 1;

R = PEG.
```

FIG. 381

```
CHO, BHK, 293 cells, Vero expressed tPA a-g, n, p = 1; h = 1 to 3; j-m, i, (independently selected) = 0 or 1; r-u (independently selected) = 0 to 1; q, o, v-y = 0.
```

alpha and beta Mannosidases
 CMP-SA, ST3Gal3
 Galactosyltransferase, UDP-Gal-PEG

```
a-g, n=1; h=1 to 3;
i, r-u (independently selected) = 0 or 1; o=1;
q, p,-v-y=0; j-m (independently selected) = 0 or 1;
R^2 = Gal-PEG
```

FIG. 38J

Plant expressed tPA

- 1. hexosaminidase,
- 2. alpha mannosidase and

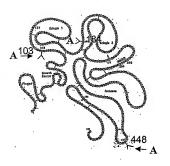
xylosidase

3. GlcNAc transferase, UDP-GlcNAc-PEG

A = B; a-d, f, h, j-n, s, u, v-y = 0; e, g, i, r, t (independently selected) = 0; q = 1; R' = GlcNAc-PEG.

FIG. 38K

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$$\mathbf{A} \longleftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & \operatorname{Man} \left([\operatorname{GlcNAc-(Gal)}_{a}]_{a} - (\operatorname{Sia})_{j} - (\operatorname{R})_{v} \right)_{r} \\ (\operatorname{GlcNAc-GlcNAc-Man} & \left[[\operatorname{GlcNAc-(Gal)}_{b}]_{f} - (\operatorname{Sia})_{k} - (\operatorname{R})_{w} \right]_{s} \\ (\operatorname{GlcNAc-(Gal)}_{d}]_{g} - (\operatorname{Sia})_{l} - (\operatorname{R})_{x} \right)_{t} \\ \left[[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \right)_{y} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \end{bmatrix}_{t} \\ \left[[\operatorname{GlcNAc-(Gal)}_{d}]_{h} - (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \right)_{y} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{m} - (\operatorname{R})_{y} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{m} - (\operatorname{Gal})_{m} - (\operatorname{R})_{y} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{m} - (\operatorname{Gal})_{m} - (\operatorname{Gal})_{m} - (\operatorname{Gal})_{m} \\ (\operatorname{GlcNAc-(Gal)}_{d})_{m} - (\operatorname{Gal})_{m} - (\operatorname{Gal})_{m} - (\operatorname{Gal})_{m} \\ (\operatorname{Gal})_{m} - ($$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

 Sialidase
 CMP-SA-PEG (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; R = PEG.

FIG. 38M

CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

 Sialidase
 CMP-SA-PEG (1.2 mol eq), ST3Gal3
 CMP-SA (16 mol eq), ST3Gal3

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 38N

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```
NSO expressed TNK tPA
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.
```

1. Sialidase and α-galactosidase

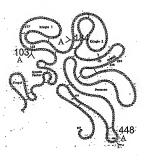
2. Galactosyltransferase, UDP-Gal

▼ 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 380

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$$\mathbf{A} \leftarrow \begin{bmatrix} [\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{a}]_{a}^{-} \cdot (\mathrm{Sia})_{j}^{-} \cdot (\mathrm{R})_{v} \end{bmatrix}_{r} \\ [\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{b}]_{f}^{-} \cdot (\mathrm{Sia})_{k}^{-} \cdot (\mathrm{R})_{w} \end{bmatrix}_{g} \\ [\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{d}]_{g}^{-} \cdot (\mathrm{Sia})_{l}^{-} \cdot (\mathrm{R})_{x} \end{bmatrix}_{t} \\ [\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{d}]_{h}^{-} \cdot (\mathrm{Sia})_{m}^{-} \cdot (\mathrm{R})_{y} \end{bmatrix}_{u} \\ (\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{d}]_{h}^{-} \cdot (\mathrm{Sia})_{m}^{-} \cdot (\mathrm{R})_{y} \\ (\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{d})_{m}^{-} \cdot (\mathrm{Sia})_{m}^{-} \cdot (\mathrm{R})_{y} \\ (\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{d})_{m}^{-} \cdot (\mathrm{Sia})_{m}^{-} \cdot (\mathrm{R})_{y} \\ (\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{d})_{m}^{-} \cdot (\mathrm{Gal})_{d} \\ (\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{d})_{m}^{-} \cdot (\mathrm{Gal})_{m}^{-} \cdot (\mathrm{Gal})_{d} \\ (\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{d})_{m}^{-} \cdot (\mathrm{Gal})_{m}^{-} \cdot (\mathrm{Gal})_{d} \\ (\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{d})_{m}^{-} \cdot (\mathrm{Gal})_{m}^{-} \cdot (\mathrm{Gal})_{d} \\ (\mathrm{GlcNAc}\text{-}(\mathrm{Gal})_{m}^{-} \cdot (\mathrm{Gal})_{m}^{-} \cdot (\mathrm{Gal}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

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```
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    Sialidase
```

2. CMP-SA-PEG (16 mol eq), ST3Gal3

3, CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 38Q

```
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    2. H<sub>4</sub>N<sub>2</sub>-PEG
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

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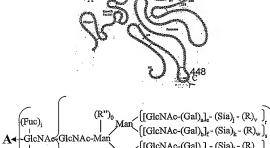
CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.

1. CMP-SA, α2,8-ST

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 38S

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a-d, i, n-y (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 100.

R = modifying group, mannose, oligo-mannose;

R'=H, glycosyl residue, modifying group, glycoconjugate.

R" = glycosyl residue.

```
Insect cell expressed TNK tPA a-d, f, h, j-m, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
    GNT's 1,2,4,5, UDP-GlcNAc
    Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1;
j-m = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 38U

```
Yeast expressed TNK tPA a-m = 0; q-y (independently selected) = 0 to 1; p = 1; R (branched or linear) = Man, oligomannose.
```

```
    Endoglycanase
    Galactosyltransferase, UDP-Gal-PEG
```

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-PEG.
```

FIG. 38V

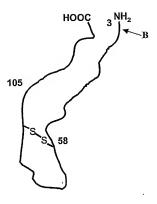
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CHO, BHK, 293 cells, Vero expressed TNK tPA a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

```
1. CMP-SA-linker-Gal-UDP,
ST3Gal3
2. Galactosyltransferase, anti-TNF
IG chimera produced in CHO.
```

a-m, r-u (independently selected) = 0 or 1; p, q = 1; n = 0; v-y (independently selected) = 0 or 1; R = linker-anti-TNF IG chimera protein.

FIG. 38W



$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_{b} \\ -\mathrm{GalNAc} - (\mathrm{Gal})_{a} - (\mathrm{Sia})_{c} - (\mathrm{R})_{d} \end{bmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, mannose, oligomannose.

FIG. 39A

CHO, BHK, 293 cells, Vero expressed IL-2 a-c, e (independently selected) = 0 or 1; d = 0

Sialidase
 CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 39B

Insect cell expressed IL-2 a, e (independently selected) = 0 or 1; b, c, d = 0.

Galactosyltransferase, UDP-Gal
 CMP-SA-PEG, ST3Gal1

a, c, d, e (independently selected) = 0 or 1; R = PEG.

FIG. 39C

```
E. coli expressed IL-2
a-e = 0.

1. GalNAc Transferase, UDP-GalNAc
2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1;
a, b = 0; R = PEG.
```

FIG. 39D

```
NSO expressed IL-2
a, e (independently selected) = 0 or 1;
b, c, d = 0

1. CMP-SA-levulinate, ST3Gall
2. H_4N_2-PEG

a, c, d, e (independently selected) = 0 or 1;
b = 0; R = PEG.
```

FIG. 39E

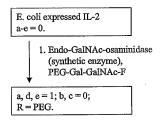


FIG. 39F

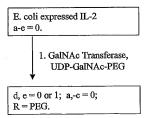


FIG. 39G

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2 peptides
A and A' - N-linked sites
B - O-linked sites

a-d, i, n-u (independently selected) = 0 or 1. aa, bb (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 20. v-z = 0; R = polymer, glycoconjugate.

FIG. 40A

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```
CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII. e-h = 1 to 4; aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1; v-z=0.
```

```
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
```

```
e-h = 1 to 4;
aa, bb, a-d, i, n, q-u (independently selected) = 0 or 1;
o, p, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40B

```
CHO, BHK, 293S cells, Vero, MDCK, 293S, HEKC expressed Factor VIII. e-h = 1 to 4; aa, bb, a-d, j-m, i, n-u (independently selected) = 0 or 1; v-z = 0.
```

```
1. Sialidase
2. CMP-SA-PEG, ST3Gal3
3. ST3Gal1, CMP-SA
```

```
e-h = 1 to 4;
aa, bb, a-d, i, n, p-u (independently selected) = 0 or 1;
o, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40C

CHO, BHK, 293s cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1;
v-z = 0.

1. CMP-SA-PEG, ST3Gal3

e-h = 1 to 4; aa, bb, a-d, i, n-u (independently selected) = 0 or 1; z = 0; j-m, v-y (independently selected) = 0 or 1; R = PEG.

FIG. 40D

CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, a-d, j-m, i, n-u (independently selected) 0 or 1;
v-z = 0.

1. CMP-SA-PEG, ST3Gal1

e-h = 1 to 4; aa, bb, a-d, i, n-u (independently selected) = 0 or 1; z = 0; j-m, v-y (independently selected) = 0 or 1; R = PEG.

FIG. 40E

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CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII. e-h = 1 to 4; aa, bb, a-d, j-m, i, n-u (independently selected)=0 or 1; v-z = 0.

1. CMP-SA-PEG, α2,8-ST

e-h = 1 to 4; aa, bb, a-d, i, n-y (independently selected) = 0 or 1; z = 0; j-m (independently selected) = 0 to 2; v-y (independently selected) = 1, when j-m (independently selected) is 2; R = PEG.

FIG. 40F

PCT/US02/32263 WO 03/031464

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2 peptides A or A' - N-linked sites

structures of A.

a-d, i, n-u, (independently selected) = 0 or 1. aa, bb, cc, dd (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. i-m (independently selected) = 0 to 20. v-z = 0;R = modifying group, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 40G

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```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

CMP-SA-levulinate, ST3Gal3,
 2. H₄N₂-PEG

```
e-h = 1 to 4;
aa, bb, cc, a-d, i, n-u (independently selected) = 0 or 1;
dd, z = 0; j-m, v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 40H

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

endo-H
 galactosyltransferase, UDP-Gal-PEG

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z = 0; R' = -Gal-PEG.
```

FIG. 401

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```
CHO, BHK, 293S cells, Vero, MDCK, HEKC
expressed Factor VIII.
e-h = 1 to 4;
ad, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.

1. ST3Gal3, CMP-SA
2. endo-H
3. galactosyltransferase, UDP-Gal-PEG
```

```
e-h = 1 to 4;
aa, bb, dd, a-d, i, j-u (independently selected) = 0 or 1;
cc, v-z=0; R'=-Gal-PEG.
```

FIG. 40J

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

```
    mannosidases
    GNT 1 & 2, UDP-GlcNAc
```

3. galactosyltransferase, UDP-Gal-PEG

```
e-h=1 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z=0; R=PBG.
```

FIG. 40K

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```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

```
1. mannosidases
```

- 2. GNT-1,2, 4 & 5; UDP-GlcNAc
- ↓ 3. galactosyltransferase, UDP-Gal
 4. ST3Gal3, CMP-SA

```
e-h = 1 to 4;
aa, bb, cc, a-d, i, j-q (independently selected) = 0 or 1;
dd, v-z=0.
```

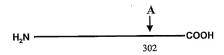
FIG. 40L

```
CHO, BHK, 293S cells, Vero, MDCK, HEKC expressed Factor VIII.
e-h = 1 to 4;
aa, bb, cc, a-d, j-m, i, n-u (independently selected) = 0 or 1;
dd, v-z = 0.
```

```
    mannosidases
    GNT-1, UDP-GlcNAc-PEG
```

```
e-h = 0 to 4;
aa, a-d, i, j-y (independently selected) = 0 or 1;
bb, cc, dd, z = 0.
```

FIG. 40M



$$\mathbf{A} = \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{a} \end{bmatrix}_{a}^{-} \cdot \left(\operatorname{Sia} \right)_{j} - \left(\operatorname{R} \right)_{v} \right)_{r}^{r}}_{\left[\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{b} \end{bmatrix}_{l}^{-} \cdot \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right]_{s}^{r}} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{l}^{-} \cdot \left(\operatorname{Sia} \right)_{k} - \left(\operatorname{R} \right)_{w} \right)_{l}^{r}}_{\left[\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{m} - \left(\operatorname{R} \right)_{y} \right)_{u}}_{q} \\ \underbrace{\left(\begin{bmatrix} \operatorname{GlcNAc-(Gal)}_{d} \end{bmatrix}_{b}^{-} \cdot \left(\operatorname{Sia} \right)_{u} - \left(\operatorname{R} \right)_{u} - \left(\operatorname{Gal} \right)_{u} - \left(\operatorname{R} \right)_{u} - \left(\operatorname{Sia} \right)_{u} - \left(\operatorname{R} \right)_{u} - \left(\operatorname{Gal} \right)_{u} - \left(\operatorname{G$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer.

FIG. 41A

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CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

```
    Sialidase
    CMP-SA-PEG (16 mol eq),
ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 41B

CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

```
1. Sialidase
2. CMP-SA-PEG (1.2 mol eq),
ST3Gal3
3. CMP-SA (16 mol eq), ST3Gal3
```

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 41C

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```
NSO expressed Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.
```

```
1. Sialidase and α-galactosidase
2. α-Galactosyltransferase, UDP-Gal
```

★ 3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 41D

```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y=0.
```

```
1. Sialidase
2. CMP-SA-PEG (16 mol eq),
ST3Gal3
3. CMP-SA. ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 41E

```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>A</sub>N<sub>2</sub>-PEG
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 41F

```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.
```

```
1. CMP-SA, α2,8-ST
```

```
a-d, i, q-u (independently selected) = 0 or 1;
e-h = 1;
j-m (independently selected) = 0-20;
v-y (independently selected) = 0.
```

FIG. 41G



$$\mathbf{A} = (\operatorname{Fuc})_{i} \\ \operatorname{GlcNAc-Gal})_{a} \cdot (\operatorname{Sia})_{i} - (\operatorname{R})_{v} \\ \operatorname{GlcNAc-Man} \\ \left[(\operatorname{GlcNAc-(Gal)}_{a})_{g} \cdot (\operatorname{Sia})_{i} - (\operatorname{R})_{v} \right]_{i} \\ \left[(\operatorname{GlcNAc-(Gal)}_{a})_{g} \cdot (\operatorname{Sia})_{i} - (\operatorname{R})_{x} \right]_{t} \\ \left((\operatorname{R}')_{n} \right) \\ \left[(\operatorname{GlcNAc-(Gal)}_{d})_{h} \cdot (\operatorname{Sia})_{m} - (\operatorname{R})_{y} \right]_{u} \\ q_{p}$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 41H

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```
Insect cell expressed Urokinase. a-d, f, h, j-n, s, u, v-y = 0; e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1;
j-n = 0; v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 411

```
Yeast expressed Urokinase.

a-n=0;

q-y (independently selected) = 0 to 1;

p=1; R (branched or linear) = Man, oligomannose.
```

```
    Endoglycanase
    Galactosyltransferase, UDP-Gal
    CMP-SA-PEG, ST3Gal3
```

```
a-m, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.
```

FIG. 41J

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```
CHO, BHK, 293 cells, Vero expressed Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; n, v-y=0.
```

```
    CMP-SA-linker-SA-CMP, ST3Gal3
```

2. ST3Gal1, desialylated Urokinase produced in CHO.

3. CMP-SA, ST3Gal3, ST3Gal1

```
a-m, q-u (independently selected) = 0 or 1;
p = 1; n = 0;
v-y (independently selected) = 0 or 1;
R = linker-Urokinase.
```

FIG. 41K

```
Isolated Urokinase.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0; n = 0;
Sia (independently selected) = Sia or SO<sub>4</sub>;
Gal (independently selected) = Gal or GalNAc;
GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc.
```

sulfohydrolase
 CMP-SA-PEG, sialyltransferase

```
a-d, i-m, q-u (independently selected) = 0 or 1; 
 n=0; e-h = 1; Sia = Sia; Gal (independently selected) = Gal or GalNAc; GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc. v-y (independently selected) = 0 or 1; 
 R=PEG.
```

FIG. 41L

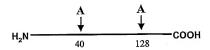
Isolated Urokinase. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; n = 0; v-y = 0; Sia (independently selected) = Sia or SO_4 ; Gal (independently selected) = Gal or GalNAc; GloNAc (independently selected) = GloNAc or GloNAc-Fuc.

1. sulfohydrolase, hexosaminidase

2. UDP-Gal-PEG, galactosyltransferase

a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-n = 0; Gal (independently selected) = Gal; GlcNAc (independently selected) = GlcNAc or GlcNAc-Fuc; v-y (independently selected) = 0 or 1; R = PEG.

FIG. 41M



$$\begin{array}{c} \text{(Fuc)}_{i} \\ \text{(Fuc)}_{i} \\ \text{(GlcNAc-(Gal)}_{b}]_{c}^{-} \text{(Sia)}_{j} - (R)_{v} \\ \text{([GlcNAc-(Gal)}_{b}]_{r} - (Sia)_{k} - (R)_{w} \\ \text{([GlcNAc-(Gal)}_{d}]_{p}^{-} \text{(Sia)}_{l} - (R)_{x} \\ \text{([GlcNAc-(Gal)}_{d}]_{h}^{-} \text{(Sia)}_{m} - (R)_{y} \\ \text{([GlcNAc-(Gal)}_{d}]_{h}^{-} \text{(Sia)}_{m} - (R)_{y} \\ \text{([GlcNAc-(Gal)}_{d}]_{h}^{-} \text{(Sia)}_{m} - (R)_{y} \\ \text{(Sia)}_{l} - (R)_{y} \\ \text{($$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 42A

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
1. Sialidase
2. CMP-SA-PEG (16 mol eq),

This statement of the statement o
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 42B

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-PEG (1.2 mol eq), ST3Gal3
    CMP-SA (16 mol eq), ST3Gal3
```

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 42C

```
NSO expressed DNase I.
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y = 0;
Sia (independently selected) = Sia or Gal.
```

```
    Sialidase and α-galactosidase
    α-Galactosyltransferase, UDP-Gal
```

3. CMP-SA-PEG, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = PEG.
```

FIG. 42D

```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y = 0.
```

```
    Sialidase
    CMP-SA-PEG (16 mol eq), ST3Gal3
```

3, CMP-SA, ST3Gal3

```
a-d, i-m, q-u (independently selected) = 0 or 1;
e-h = 1; v-y (independently selected) = 0 or 1;
R = PEG.
```

FIG. 42E

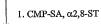
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.

```
    CMP-SA-levulinate, ST3Gal3,
buffer, salt
    H<sub>4</sub>N<sub>2</sub>-PEG
```

a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; v-y (independently selected) = 0 or 1; R = PEG.

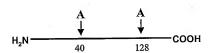
FIG. 42F

CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h=1; v-y=0.



a-d, i, q-u (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-20; v-y (independently selected) = 0.

FIG. 42G



$$\mathbf{A} = \begin{bmatrix} (\operatorname{Fuc})_i \\ \operatorname{GlcNAc-Gal})_a \end{bmatrix}_c - (\operatorname{Sia})_j - (\operatorname{R})_v \end{bmatrix}_r \\ \left[[\operatorname{GlcNAc-(Gal)}_b]_f - (\operatorname{Sia})_k - (\operatorname{R})_w \end{bmatrix}_s \\ \left[[\operatorname{GlcNAc-(Gal)}_b]_g - (\operatorname{Sia})_l - (\operatorname{R})_x \end{bmatrix}_t \\ \left[[\operatorname{GlcNAc-(Gal)}_d]_h - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \right]_q \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{R})_y \end{bmatrix}_u \\ = \begin{bmatrix} \operatorname{GlcNAc-(Gal)}_b \end{bmatrix}_r - (\operatorname{Sia})_m - (\operatorname{GlcNAc-(Gal)}_r - (\operatorname{Gal})_r - (\operatorname{G$$

a-d, i, n, p-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0;

R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 42H

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```
Insect cell expressed DNase I.
a-d, f, h, j-n, s, u, v-y=0;
e, g, i, q, r, t (independently selected) = 0 or 1.
```

```
1. GNT's 1,2,4,5, UDP-GlcNAc
2. Galactosyltransferase, UDP-Gal-PEG
```

```
a-i, q-u (independently selected) = 0 or 1; j-n = 0;
v-y (independently selected) = 1,
when e-h (independently selected) is 1;
R = PEG.
```

FIG. 421

```
Yeast expressed DNase I.

a-n = 0;

q-y (independently selected) = 0 to 1;

p = 1; R (branched or linear) = Man, oligomannose.
```

- Endoglycanase
 Galactosyltransferase, UDP-Gal
- 3. CMP-SA-PEG, ST3Gal3

a-n, p-y = 0; n (independently selected) = 0 or 1; R' = -Gal-Sia-PEG.

FIG. 42J

PCT/US02/32263

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```
CHO, BHK, 293 cells, Vero expressed DNase I. a-d, i-m, q-u (independently selected) = 0 or 1; e-h = 1; n, v-y = 0.
```

- 1. CMP-SA-linker-SA-CMP, ST3Gal3
- 2. ST3Gal1, desialylated alpha-1-Proteinase inhibitor.
- 3, CMP-SA, ST3Gal3, ST3Gal1

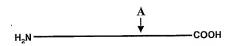
```
a-m, q-u (independently selected) = 0 or 1;

p = 1; n = 0;

v-y (independently selected) = 0 or 1;

R = linker- alpha-1-Proteinase inhibitor.
```

FIG. 42K



$$(Fuc)_{i} \\ A \leftarrow GlcNAc - GlcNAc - Man \\ (R')_{n} \\ (R')_{n} \\ (GlcNAc - (Gal)_{a}]_{e} - (Sia)_{i} - (R)_{v} \\ [[GlcNAc - (Gal)_{b}]_{r} - (Sia)_{k} - (R)_{w}]_{s} \\ [[GlcNAc - (Gal)_{d}]_{r} - (Sia)_{l} - (R)_{x} \\ [[GlcNAc - (Gal)_{d}]_{h} - (Sia)_{m} - (R)_{y} \\ [[GlcNAc - (Gal)_{d}]_{h} - (R)_{y} \\ [[GlcNac$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y=0; z=0 or 1; R = modifying group, mannose, oligo-mannose; R'=H, glycosyl residue, modifying group, glycoconjugate.

FIG. 43A

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```
CHO, BHK, 293 cells, Vero expressed Insulin.

a-m, r-u (independently selected) = 0 or 1;

n = 0; v-y = 0; z = 1.

1. Sialidase
2. CMP-SA-PEG, ST3Gal3

a-m, r-u (independently selected) = 0 or 1;
```

```
a-ii, 1-ii (independently selected) = 1,
when j-m (independently selected) is 1;
n=0; R=PEG; z=1.
```

FIG. 43B

```
Insect cell expressed Insulin.
a-h, j-n, s-y = 0;
i, r (independently selected) = 0 or 1; z = 1.

1. GNT's 1&2, UDP-GlcNAc-PEG
```

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 43C

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Yeast expressed Insulin.

a-n=0; r-y (independently selected) = 0 to 1;

z=1;

R (branched or linear) = Man, oligomannose or polysaccharide.

1, Endo-H

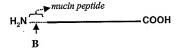
2. Galactosyltransferase, UDP-Gal-PEG

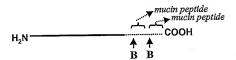
a-m, r-z=0; n = 1; R' = -Gal-PEG.

FIG. 43D

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$$\mathbf{B} \quad \blacktriangleleft \begin{pmatrix} (\operatorname{Sia})_{b} \\ {}^{1} \\ \operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_{c} - (\operatorname{R})_{d} \end{pmatrix}_{c}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 43E

CHO, BHK, 293 cells, Vero expressed insulinmucin fusion protein.

a-c, e (independently selected) = 0 or 1; d = 0

- 1. Sialidase
- 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 43F

Insect cell expressed Insulin-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

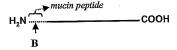
FIG. 43G

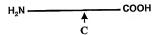
E. coli expressed Insulin-mucin fusion protein. a-e=0.

- 1. GalNAc Transferase, UDP-GalNAc 2. CMP-SA-PEG, sialyltransferase
- c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 43H







$$\mathbf{B} \quad \blacktriangleleft \stackrel{\mathrm{(Sia)}_{b}}{\left(\stackrel{\cdot}{\operatorname{GalNAc-(Gal)}_{a^{-}}(\operatorname{Sia})_{c^{-}}(\mathbb{R})_{d} \right)_{c}}}$$

a-c, e (independently selected) = 0 or 1; d=0; R=modifying group, mannose, oligo-mannose.

FIG. 431

E. coli expressed Insulin-mucin fusion protein. a-e, $\mathbf{n} = \mathbf{0}$.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 43J

E. coli expressed Insulin-mucin fusion protein. a-e. n=0.

- 1. GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
 3. CMP-SA, ST3Gal3
- d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

FIG. 43K

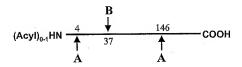
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E. coli expressed Insulin (N)—no mucin peptide. a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP 2. ST3Gal3, asialo-transferrin 3. CMP-SA, ST3Gal3

a-e = 0; n = 1;R' = linker-transferrin.

FIG. 43L



$$A \leftarrow \begin{bmatrix} (\operatorname{Fuc})_i & \operatorname{Man} \left([\operatorname{GlcNAc-(Gal)}_{a}]_e^- (\operatorname{Sia})_j - (R)_v \right)_r \\ -\operatorname{GlcNAc-GlcNAc-Man} & \operatorname{Man} \left([\operatorname{GlcNAc-(Gal)}_{b}]_r^- (\operatorname{Sia})_k - (R)_w \right)_r \\ \operatorname{Man} \left([\operatorname{GlcNAc-(Gal)}_{d}]_p^- (\operatorname{Sia})_l - (R)_x \right)_t \\ \left([\operatorname{GlcNAc-(Gal)}_{d}]_h^- (\operatorname{Sia})_m^- (R)_y \right)_u \\ -\operatorname{GalNAc-(Gal)}_{a} - (\operatorname{Sia})_p^- (R)_z \end{bmatrix}_{aa}$$

a-d, i, n-u, aa (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-m (independently selected) = 0 to 100. v-y = 0; R = polymer, glycoconjugate.

FIG. 44A

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CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

 Sialidase
 CMP-SA-linker-lipid-A, ST3Gal3

```
a-d, i-m, q-u, aa (independently selected) = 0 or 1;
o, p, z = 0; n, e-h = 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
R = linker-lipid-A.
```

FIG. 44B

CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

- sialidase
- 2. CMP-SA-linker-tetanus toxin, ST3Gal1
- 3, CMP-SA, ST3Gal3

a-d, i-m, p-u, z, as (independently selected) = 0 or 1; o, v-y = 0; n, e-h = 1; R = tetanus toxin.

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```
NSO expressed M-antigen.
a-d, i-n, o-u, aa (independently selected) = 0 or 1;
e-h = 1; v-z = 0;
Sia (independently selected) = Sia or Gal.
```

```
1. α-galactosidase
2. CMP-SA, ST3Gal3
2. CMP-SA-KLH, ST3Gal1
```

```
a-d, i-n, p-u, z, aa (independently selected) = 0 or 1;
e-h = 1; o, v-y = 0;
z = 1, when p = 1;
R = KLH.
```

FIG. 44D

```
Yeast expressed M-antigen.
a-p, z = 0; q-y, aa (independently selected) = 0 to 1;
R (branched or linear) = Man, oligomannose;
GalNAc = Man.
```

1. α1,2-mannosidase 2. GNT 1,

UDP-GlcNAc-linker-diphtheria toxin.

```
e, q, l, m, r, t, u, v, aa (independently selected) =0 or 1; a-d, f-h, j, k, n-p, s, w-z = 0; Sia = Man; R = linker-diphtheria toxin.
```

FIG. 44E

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CHO, BHK, 293 cells, Vero expressed M-antigen. a-d, i-m, o-u, aa (independently selected) = 0 or 1; n, e-h = 1; v-z = 0.

1. CMP-SA-levulinate, ST3Gal3, 2. H₄N₂-linker-DNA

a-d, i-m, o-y, as (independently selected) = 0 or 1; z = 0; n, e-h = 1; R = linker-DNA.

FIG. 44F

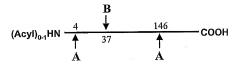
CHO, BHK, 293 cells, Vero expressed M-antigen a-d, i-n, o-u, aa (independently selected) = 0 or 1; e-h=1; v-z=0.

1. CMP-SA, poly-α2,8-ST

a-d, i, n-u, aa (independently selected) = 0 or 1; e-h = 1; j-m (independently selected) = 0-100; y-z (independently selected) = 0.

FIG. 44G

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} \\ -\operatorname{GlcNAc}_{i} \\ -\operatorname{GlcNAc}_{i}$$

$$\mathbf{B} \quad \begin{array}{c} \text{(Sia)}_{\text{o}} \\ \text{-GalNAc-(Gal)}_{\text{n}}\text{-(Sia)}_{\text{p}}\text{- (R)}_{\text{z}} \\ \text{as} \end{array}$$

a-d, i, n, q-u, aa, bb, (independently selected) = 0 or 1. e-h (independently selected) = 0 to 6. j-p (independently selected) = 0 to 100. Cc, v-y = 0; R = modifying group, mannose, oligo-mannose. R'= H, glycosyl residue, modifying group, glycoconiugate.

FIG. 44H

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```
Insect cell expressed M-antigen.

a-d, f, h, j-m, o, p, s, u, v-z, cc = 0;

bb = 1;

e, g, i, n, q, r, t, aa (independently selected) = 0 or 1.
```

1. GNT-2, UDP-GlcNAc-linker-Neisseria protein

a, c, e, g, i, n, q, r, t, v, x, aa (independently selected) = 0 or 1; b, d, f, h, j-p, s, u, w, y, z, cc = 0; bb = 1; R = -linker-Neisseria protein.

FIG. 441

Yeast expressed M-antigen. a-p, z, cc = 0; q-y, aa (independently selected) = 0 to 1; bb = 1; R (branched or linear) = Man, oligomannose; GalNAc = Man.

- 1. Endoglycanase
- 2. Galactosyltransferase,
 UDP-Gal-linker-Neisseria protein

a-p, r-z, bb = 0; q, aa, cc (independently selected) = 0 or 1; R' = -Gal-linker-Neisseria protein.

FIG. 44J

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```
Yeast expressed M-antigen.
```

a-p, z, cc = 0;

q-y, aa (independently selected) = 0 to 1; bb = 1;

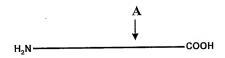
R (branched or linear) = Man, oligomannose;

GalNAc = Man.

- 1, mannosidases
- 2. GNT 1 & 2, UDP-GlcNAc
- 3. UDP-Gal, Galactosyltransferase,
- 4. CMP-SA, sialyltransferase

a, c, e, g, j, 1, q, r, t, aa (independently selected) = 0 or 1; b, d, f, h, k, m-p, s, u-z, cc = 0; bb = 1.

FIG. 44K



$$\begin{array}{c} \text{(Fuc)}_{i} \\ \text{A} \leftarrow \text{GlcNAc-Man} \\ \text{(R')}_{n} \end{array} \\ \text{Man} \underbrace{\begin{bmatrix} [\text{GlcNAc-(Gal)}_{a}]_{e^{-}} (\text{Sia})_{i} - (R)_{w} \end{bmatrix}_{r}}_{\begin{bmatrix} [\text{GlcNAc-(Gal)}_{b}]_{r} - (\text{Sia})_{k} - (R)_{w} \end{bmatrix}_{s}}_{\text{Man}} \\ \underbrace{\begin{bmatrix} [\text{GlcNAc-(Gal)}_{d}]_{g^{-}} (\text{Sia})_{r} - (R)_{x} \end{bmatrix}_{t}}_{\text{Man}} \\ \underbrace{\begin{bmatrix} [\text{GlcNAc-(Gal)}_{d}]_{h^{-}} (\text{Sia})_{m^{-}} (R)_{y} \end{bmatrix}_{u}}_{z} \\ \\ \text{Example 1} \\ \text{Man} \end{aligned}$$

a-d, i, r-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

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CHO, BHK, 293 cells, Vero expressed Growth Hormone. a-m, r-u (independently selected) = 0 or 1; n=0; v-y=0; z=1.

- Sialidase
 CMP-SA-PEG, ST3Gal3
- a-m, r-u (independently selected) = 0 or 1; v-y (independently selected) = 1, when j-m (independently selected) is 1; n = 0; R = PEG; z = 1.

FIG. 45B

```
Insect cell expressed growth hormone.
a-h, j-n, s-y = 0;
i, r (independently selected) = 0 or 1; z = 1.
```

1. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected)= 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 45C

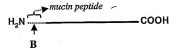
Yeast expressed growth hormone. a-n = 0; r-y (independently selected) = 0 to 1; z = 1; R (branched or linear) = Man, oligomannose or polysaccharide.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z= 0; n = 1; R' = -Gal-PEG.

FIG. 45D





$$\mathbf{B} \leftarrow \begin{bmatrix} (\mathrm{Sia})_b \\ -\mathrm{GaINAc-}(\mathrm{GaI})_a - (\mathrm{Sia})_c - (\mathrm{R})_d \end{bmatrix}_c$$

a-c, e (independently selected) = 0 or 1; d = 0; R = modifying group, mannose, oligomannose.

FIG. 45E

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CHO, BHK, 293 cells, Vero expressed growth hormone-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d = 0

Sialidase
 CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 45F

Insect cell expressed Growth Hormone-mucin fusion protein.

a, e (independently selected) = 0 or 1; b, c, d = 0.

Galactosyltransferase, UDP-Gal-PEG

a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

FIG. 45G

E. coli expressed growth hormone-mucin fusion protein. a-e=0.

-- 0.

- GalNAc Transferase, UDP-GalNAc
- 2. CMP-SA-PEG, sialyltransferase

c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 45H

E. coli expressed growth hormone-mucin fusion protein.

a-e, n = 0.

GalNAc Transferase,
 UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 451

E. coli expressed growth hormone-mucin fusion protein.

a-e, n=0.

- GalNAc Transferase, UDP-GalNAc-linker-SA-CMP
 ST3Gal3, asialo-transferrin
- ▼ 3. CMP-SA, ST3Ga13

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

FIG. 45J

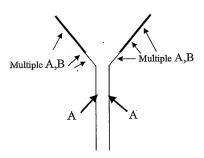
E. coli expressed growth hormone (N)—no mucin peptide.

a-e, n = 0.

- 1. NHS-CO-linker-SA-CMP
- 2. ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Gal3

a-e=0; n=1; R'=linker-transferrin.

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$$A \leftarrow \begin{bmatrix} (\operatorname{Fuc})_{i} & \operatorname{Man} \left([\operatorname{GlcNAc-(Gal)}_{a}]_{o}^{-} (\operatorname{Sia})_{j}^{-} (\operatorname{R})_{v} \right)_{i} \\ -\operatorname{GlcNAc-Man} & \operatorname{Man} \left([\operatorname{GlcNAc-(Gal)}_{o}]_{f}^{-} (\operatorname{Sia})_{k}^{-} (\operatorname{R})_{w} \right)_{i} \\ -\operatorname{R'}_{i} & \operatorname{Man} \left([\operatorname{GlcNAc-(Gal)}_{o}]_{g}^{-} (\operatorname{Sia})_{i}^{-} (\operatorname{R})_{x} \right)_{t} \\ -\operatorname{R'}_{i} & \operatorname{GlcNAc}_{ww} & \left[[\operatorname{GlcNAc-(Gal)}_{o}]_{g}^{-} (\operatorname{Sia})_{m}^{-} (\operatorname{R})_{y} \right]_{u} \\ -\operatorname{R'}_{i} & \operatorname{GlcNAc-(Gal)}_{m}^{-} (\operatorname{Sia})_{p}^{-} (\operatorname{R})_{zz} \right)_{q} \\ -\operatorname{GalNAc-(Gal)}_{m}^{-} (\operatorname{Sia})_{p}^{-} (\operatorname{R})_{zz} \right]_{q}$$

a-d, i-m, q-u, w, z, nn, ww, zz (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4.

n, v-y = 0;

R = modifying group, mannose, oligo-mannose;

R'=H, glycosyl residue, modifying group, glycoconjugate.

FIG. 46A

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1;
n = 1; v-z = 0.

```
    CMP-SA, ST3Gal1
    galactosyltransferase, UPD-Gal
    CMP-SA-PEG, ST3Gal3
```

a-m, o-u, v-y, as (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 46B

CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n=1; v-z=0.

1. sialidase
 ▼ 2. CMP-SA-PEG, ST3Gal1

a-i, p-u, z, aa (independently selected) = 0 or 1; n = 1; o, j-m, v-y = 0; R = PEG.

FIG. 46C

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CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion.
a-m, o-u, aa (independently selected) = 0 or 1; n = 1; v-z = 0.

1. galactosyltransferase, UPD-Gal-PEG

a-m, o-u, v-y, aa (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 46D

CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n = 1; $v \cdot z = 0$.

- CMP-SA, ST3Gal1
- 2. galactosyltransferase, UPD-Gal-PEG

a-m, o-u, v-y, aa (independently selected) = 0 or 1; n = 1; z = 0; R = PEG.

FIG. 46E

```
CHO, BHK, 293 cells, Vero or transgenic animals expressed TNF Receptor IgG Fusion.

a-m, o-u, aa (independently selected) = 0 or 1;

n = 1; v-z = 0.
```

```
1. CMP-SA-levulinate, ST3Gal1
2. H<sub>4</sub>N<sub>2</sub>-PEG
```

```
a-m, o-u, v-y, as (independently selected) = 0 or 1;

n = 1; z = 0; R = PEG.
```

FIG. 46F

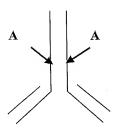
```
CHO, BHK, 293 cells, Vero expressed TNF Receptor IgG Fusion. a-m, o-u, aa (independently selected) = 0 or 1; n=1; v-z=0.
```

```
1. CMP-SA-PEG, \alpha2,8-ST
```

```
a-i, o, q-u, v-z, aa (independently selected) = 0 or 1; n = 1; j-m, p (independently selected) = 0 to 2; v-z (independently selected) = 1, when j-m, p (independently selected) is 2; R = PEG.
```

FIG. 46G

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$$\begin{array}{c} \text{(Fuc)}_{i} \\ \text{GlcNAc-Man} \\ \text{(R')}_{n} \end{array} \\ \text{(GlcNAc-Man)}_{a} \begin{bmatrix} [\text{GlcNAc-(Gal)}_{a}]_{e^{-}} (\text{Sia)}_{j^{-}} (\text{R})_{v} \\ [\text{GlcNAc-(Gal)}_{b}]_{f^{-}} (\text{Sia)}_{k^{-}} (\text{R})_{w} \end{bmatrix}_{g} \\ \text{(R')}_{n} \\ \text{(GlcNAc-(Gal)}_{d}]_{h^{-}} (\text{Sia)}_{m^{-}} (\text{R})_{y} \end{bmatrix}_{u} \\ \text{(GlcNAc-(Gal)}_{d}]_{h^{-}} (\text{Sia})_{m^{-}} (\text{R})_{y} \end{bmatrix}_{u} \\ \text{(R')}_{n} \\ \text{($$

a-d, i, l, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-k (independently selected) = 0 or 1.

M = 0 to 20.

n, v-y=0; z=0 or 1;

R= polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 47A

```
CHO, BHK, 293 cells, Vero expressed Herceptin. a, c, i (independently selected) = 0 or 1; e, g, r, t=1; b, d, f, h, j-m, n, s, u-y=0; q, z=1.
```

galactosyltransferase, UPD-Gal
 CMP-SA-toxin, ST3Gal3

```
a, c, i, j, 1 (independently selected) = 0 or 1;
e, g, r, t = 1; R = toxin;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 51,
when j, 1 (independently selected) is 1.
```

FIG. 47B

CHO, BHK, 293 cells, Vero or fungal expressed Herceptin. a, c, i (independently selected) = 0 or 1; e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.

galactosyltransferase,
 UPD-Gal-Toxin

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t=1; f, h, j-m, n, s, u-y=0;
q, z=1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

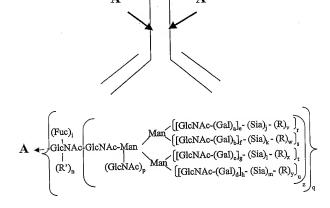
FIG. 47C

Fungi expressed Herceptin. e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

```
    1. Endo-H
    2. Galactosyltransferase, UDP-Gal
    3.. CMP-SA-radioisotope complex, ST3Gal3
```

```
a-m, r-z= 0; q, n = 1;
R' = -Gal-Sia-radioisotope complex.
```

FIG. 47D



a-d, i, p-u, (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4.

i-m (independently selected) = 0 or 1.

n, v-y=0; z=0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 48A

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```
CHO, BHK, 293 cells, Vero expressed Synagis. a, c, i (independently selected) = 0 or 1; e, g, r, t=1; b, d, f, h, j-m, n, s, u-y=0; q, z=1.
```

galactosyltransferase, UPD-Gal
 CMP-SA-PEG, ST3Gal3

```
a, c, i, j, w, (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, 1 (independently selected) is 1;
R = PEG.
```

FIG. 48B

```
CHO, BHK, 293 cells, Vero or fungal expressed Synagis. a, c, i (independently selected) = 0 or 1; e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

galactosyltransferase,
 UPD-Gal-PEG

```
a, c, i, w (independently selected) = 0 or 1;
e, g, r, t= 1; f, h, j-m, n, s, u-y= 0;
q, z= 1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.
```

Fungi expressed Synagis.

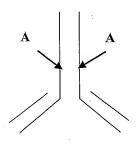
e, g, i, r, \hat{t} (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- → 3.. CMP-SA-PEG, ST3Gal3

a-m, r-z=0; q, n=1; R'=-Gal-Sia-PEG.

FIG. 48D

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_i \\ \operatorname{GlcNAc-Man} \\ | \\ (R')_n \end{bmatrix} \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_b]_e^- & (\operatorname{Sia})_j - (R)_v \end{bmatrix}_r \\ \left[(\operatorname{GlcNAc-(Gal)}_b]_f^- & (\operatorname{Sia})_k - (R)_w \end{bmatrix}_g \\ \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_x \end{bmatrix}_t \\ \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_x \end{bmatrix}_t \\ \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u \right]_{u} \\ = \left[(\operatorname{GlcNAc-(Gal)}_b]_g^- & (\operatorname{Sia})_l - (R)_y \end{bmatrix}_u$$

a-d, i, q-u, w (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 6.

j-m (independently selected) = 0 to 20.

n, v-y=0; z=0 or 1;

R = polymer, toxin, radioisotope-complex, drug, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 49A

CHO, BHK, 293 cells, Vero expressed Remicade. a, c, i (independently selected) = 0 or 1; e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.

galactosyltransferase, UPD-Gal
 CMP-SA-PEG, ST3Gal3

```
a, c, i, j, 1 (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, 1 (independently selected) is 1;
R = PEG.
```

FIG. 49B

CHO, BHK, 293 cells, Vero or fungal expressed Remicade. a, c, i (independently selected) = 0 or 1; e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.

galactosyltransferase,
 UPD-Gal-PEG

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t=1; f, h, j-m, n, s, u-y=0;
q, z=1; v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = PEG.
```

FIG. 49C

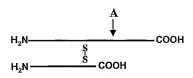
Fungi expressed Remicade.

e, g, i, r, t (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- → 3.. CMP-SA-radioisotope complex, ST3Gal3

a-m, r-z= 0; q, n = 1; R' = -Gal-Sia-radioisotope complex.

FIG. 49D



$$\mathbf{A} \leftarrow \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_s]_e^-(Sia)_j^-(R)_v]_r \\ [\operatorname{GlcNAc-(Gal)_s]_e^-(Sia)_k^-(R)_w]_s \\ [\operatorname{R''})_n \end{bmatrix} \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_s]_e^-(Sia)_j^-(R)_v]_r \\ [\operatorname{GlcNAc-(Gal)_s]_g^-(Sia)_l^-(R)_w]_s \\ [\operatorname{GlcNAc-(Gal)_s]_e^-(Sia)_l^-(R)_w]_u \end{bmatrix} \begin{bmatrix} [\operatorname{GlcNAc-(Gal)_s]_e^-(Sia)_l^-(R)_w]_s \\ [\operatorname{GlcNAc-(Gal)_s]_e^-(Sia)_l^-(R)_w]_u \end{bmatrix} \end{bmatrix}$$

a-d, i, q-u (independently selected) = 0 or 1. e-h (independently selected) = 0 to 4. j-m (independently selected) = 0 or 1. n, v-y = 0; z = 0 or 1; R = modifying group, mannose, oligo-mannose; R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 50A

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```
CHO, BHK, 293 cells, Vero expressed Reopro. a-m, r-u (independently selected) = 0 or 1; n=0;\ v-y=0;\ z=1.
```

```
    Sialidase
    CMP-SA-PEG, ST3Gal3
```

```
a-m, r-u (independently selected) = 0 or 1;
v-y (independently selected) = 1,
when j-m (independently selected) is 1;
n=0; R=PEG; z=1.
```

FIG. 50B

```
Insect cell expressed Reopro. a-h, j-n, s-y = 0; i, r (independently selected) = 0 or 1; z = 1.
```

1. GNT's 1&2, UDP-GlcNAc-PEG

```
a-d, f, h, j-n, s, u, w, y = 0;
e, g, i, r, t, v, x (independently selected) = 0 or 1;
v, x (independently selected) = 1,
when e, g (independently selected) is 1;
z = 1; R = PEG.
```

FIG. 50C

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```
Yeast expressed Reopro.
```

a-n=0; r-y (independently selected) = 0 to 1;

z=1;

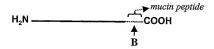
R (branched or linear) = Man, oligomannose or polysaccharide.

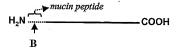
1. Endo-H

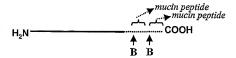
2. Galactosyltransferase, UDP-Gal-PEG

a-m, r-z=0; n = 1; R' = -Gal-PEG.

FIG. 50D







a-c, e (independently selected) = 0 or 1; d = 0; R = polymer

FIG. 50E

CHO, BHK, 293 cells, Vero expressed Reopro-mucin fusion protein. a-c, e (independently selected) = 0 or 1; d = 0

> 1. Sialidase 2. CMP-SA-PEG, ST3Gal1

a-d, e (independently selected) = 0 or 1; R = PEG.

FIG. 50F

Insect cell expressed Reopro-mucin fusion protein. a, e (independently selected) = 0 or 1; b, c, d = 0.

1. Galactosyltransferase, UDP-Gal-PEG

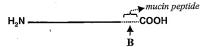
a, d, e (independently selected) = 0 or 1; b, c = 0; R = PEG.

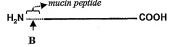
FIG. 50G

E. coli expressed Reopro-mucin fusion protein. a-e=0.

- GalNAc Transferase, UDP-GalNAc
 CMP-SA-PEG, sialyltransferase
- c, d, e (independently selected) = 0 or 1; a, b = 0; R = PEG.

FIG. 50H





$$\mathbf{B}$$

$$\begin{array}{c}
\operatorname{(Sia)_b} \\
\operatorname{(GalNAc-(Gal)_a-(Sia)_c-(R)_d}
\end{array}$$

a-c, e (independently selected) = 0 or 1; d = 0; R = polymer, linker.

FIG. 501

E. coli expressed Reopro-mucin fusion protein. a-e, n=0.

 GalNAc Transferase, UDP-GalNAc-PEG

d, e (independently selected) = 0 or 1; a-c, n = 0; R = PEG.

FIG. 50J

E. coli expressed Reopro-mucin fusion protein. a-e, n=0.

- GalNAc Transferase,
 UDP-GalNAc-linker-SA-CMP
 ST3Gal3, asialo-transferrin
- 3. CMP-SA, ST3Ga13

d, e (independently selected) = 0 or 1; a-c, n = 0; R = linker-transferrin.

FIG. 50K

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E. coli expressed Reopro(N)-no mucin peptide. a-e, n=0.

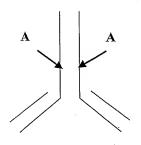
- 1. NHS-CO-linker-SA-CMP
- ST3Gal3, asialo-transferrin
 CMP-SA, ST3Gal3

a-e=0; n=1; R'=linker-transferrin.

FIG. 50L

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_i & (\operatorname{GicNAc-(Gal)_al_b^-}(\operatorname{Sia})_j - (\operatorname{R})_v)_r \\ (\operatorname{GicNAc-(Gal)_bl_f^-}(\operatorname{Sia})_i - (\operatorname{R})_w)_s \\ (\operatorname{R'})_n & (\operatorname{GicNAc-(Gal)_bl_f^-}(\operatorname{Sia})_i - (\operatorname{R})_x)_t \\ (\operatorname{GicNAc-(Gal)_bl_f^-}(\operatorname{Sia})_i - (\operatorname{R})_x)_t \\ (\operatorname{GicNAc-(Gal)_bl_f^-}(\operatorname{Sia})_m^- (\operatorname{R})_y)_u \\ z \\ z \\ q \end{bmatrix}$$

a-d, i, q-u (independently selected) = 0 or 1.
e-h (independently selected) = 0 to 4.
j-m (independently selected) = 0 or 1.
n, v-y = 0; z = 0 or 1; R = polymer, toxin, radioisotopecomplex, drug, glycoconjugate.
R' = H, sugar, glycoconjugate.

FIG. 51A

CHO, BHK, 293 cells, Vero or transgenic animal

expressed Rituxan.

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```
a, c, i (independently selected) = 0 or 1;
e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.

1. galactosyltransferase, UPD-Gal
2. CMP-SA-toxin, ST3Gal3

a, c, i, j, 1 (independently selected) = 0 or 1;
e, g, r, t = 1;
f, h, k, m, n, s, u-y = 0; q, z = 1;
v-y (independently selected) = 1,
when i, 1 (independently selected) is 1;
```

FIG. 51B

R = toxin.

```
CHO, BHK, 293 cells, Vero or fungal expressed Rituxan. a, c, e, g, i, r, t (independently selected) = 0 or 1; b, d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

galactosyltransferase,
 UPD-Gal-drug

```
a, c, i (independently selected) = 0 or 1;
e, g, r, t= 1; f, h, j-m, n, s, u-y=0; q, z = 1;
v-y (independently selected) = 1,
when a, c (independently selected) is 1;
R = toxin.
```

FIG. 51C

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```
Fungi expressed Rituxan.
```

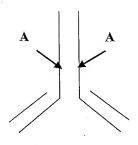
```
e, g, i, r, \hat{t} (independently selected) = 0 or 1;
a-d, f, h, j-m, n, s, u-y = 0; q, z = 1.
```

- 1. Endo-H
- 2. Galactosyltransferase, UDP-Gal
- ▼ 3. CMP-SA-radioisotope complex, ST3Gal3

```
a-m, r-z= 0; q, n = 1;
R' = -Gal-Sia-radioisotope complex.
```

FIG. 51D

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$$\mathbf{A} \leftarrow \begin{bmatrix} (\operatorname{Fuc})_i \\ \operatorname{GlcNAc-Man} \\ (R')_n \end{bmatrix} \begin{bmatrix} (\operatorname{GlcNAc-(Gal)}_a]_{a^-} & (\operatorname{Sia})_j - (R)_v \\ (\operatorname{GlcNAc-(Gal)}_b]_{f^-} & (\operatorname{Sia})_k - (R)_w \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_1 - (R)_x \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (R)_y \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b]_{g^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b)_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b)_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b)_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} & (\operatorname{Sia})_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_b)_{h^-} & (\operatorname{GlcNAc-(Gal)}_b)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{GlcNAc-(Gal)}_h)_{h^-} \\ (\operatorname{GlcNAc-(Gal)}_h)_{h^-} & (\operatorname{G$$

a-d, i, q-u (independently selected) = 0 or 1.

e-h (independently selected) = 0 to 4.

j-m (independently selected) = 0 or 1.

n, v-v=0; z=0 or 1;

R = polymer, toxin, radioisotope-complex, drug,

glycoconjugate, mannose, oligo-mannose.

R' = H, glycosyl residue, modifying group, glycoconjugate.

FIG. 51E

```
CHO, BHK, 293 cells, Vero or transgenic animal expressed Rituxan. a, c, i (independently selected) = 0 or 1; e, g, r, t = 1; b, d, f, h, j-m, n, s, u-y = 0; d, z = 1.
```

```
    galactosyltransferase, UPD-Gal
    CMP-SA-PEG, ST3Gal3
```

```
a, c, i, j, l (independently selected) = 0 or 1;
e, g, r, t = 1; f, h, k, m, n, s, u-y = 0;
q, z = 1; v-y (independently selected) = 1,
when j, l (independently selected) is 1;
R = PEG.
```

FIG. 51F

```
Fungi, yeast or CHO expressed Rituxan. e, g, i, r, t, v, x (independently selected) = 0 or 1; a-d, f, h, j-m, n, s, u, w, y = 0; q, z = 1; R (independently selected) = mannose, oligomannose, polymannose.
```

- 1. mannosidases (alpha and beta)
- GNT-I,II, UDP-GlcNAc
 Galactosyltransferase, UDP-Gal-radioisotope

a-m, r-z=0; q, n = 1; R' = -Gal-radioisotope complex.

FIG. 51G

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FIG. 52A

FIG. 52B

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro

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FIG. 53B

Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys Lys Ser Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Giu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu

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FIG. 54A

ATGACCAACAAGTGTCTCCTCCAAATTGCTCTCCTGTTGTGCTTCTCC ACTACAGCTCTTTCCATGAGCTACAACTTGCTTGGATTCCTACAAAGA AGCAGCAATTTTCAGTGTCAGAAGCTCCTGTGGCAATTGAATGGGAG GCTTGAATATTGCCTCAAGGACAGGATGAACTTTGACATCCCTGAGG AGATTAAGCAGCTGCAGCAGTTCCAGAAGGAGGACGCCGCATTGACC ATCTATGAGATGCTCCAGAACATCTTTGCTATTTTCAGACAAGATTCA TCTAGCACTGGCTGGAATGAGACTATTGTTGAGAACCTCCTGGCTAA TGTCTATCATCAGATAAACCATCTGAAGACAGTCCTGGAAGAAAAAC TGGAGAAAGAAGATTTTACCAGGGGAAAACTCATGAGCAGTCTGCAC CTGAAAAGATATTATGGGAGGATTCTGCATTACCTGAAGGCCAAGGA GTACAGTCACTGTGCCTGGACCATAGTCAGAGTGGAAATCCTAAGGA ACTTTTACTTCATTAACAGACTTACAGGTTACCTCCGAAACTGAAGAT CTCCTAGCCTGTCCCTCTGGGACTGGACAATTGCTTCAAGCATTCTTC AACCAGCAGATGCTGTTTAAGTGACTGATGGCTAATGTACTGCAAAT GAAAGGACACTAGAAGATTTTGAAATTTTTATTAAATTATGAGTTATT TTTATTTAT TTAAATTTTATTTTGGAAAATAAATTATTTTTGGTGC

FIG. 54B

Met Thr Asn Lys Cys Leu Leu Gin Ile Ala Leu Leu Leu Cys Phe Ser Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gin Arg Ser Ser Asn Phe Gin Cys Gin Lys Leu Leu Trp Gin Leu Asn Giy ArgLeu Giu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Giu Glu Ile Lys Gin Leu Gin Gin Phe Gin Lys Gu Asp Ala Ala Leu Thr Ile Tyr Giu Met Leu Gin Asn Ile Phe Ala Ile Phe Arg Gin Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gin Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn

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FIG. 55A

ATGGTCTCCCAGGCCCTCAGGCTCCTCTGCCTTCTGCTTGGGCTTCAG GGCTGCCTGGCTGCAGTCTTCGTAACCCAGGAGGAAGCCCACGGCGT CCTGCACCGGCGCGCGCGCCAACGCGTTCCTGGAGGAGCTGCGGC CGGGCTCCCTGGAGAGGGAGTGCAAGGAGGAGCAGTGCTCCTTCGA GGAGGCCCGGGAGATCTTCAAGGACGCGGAGAGGACGAAGCTGTTC TGGATTTCTTACAGTGATGGGGACCAGTGTGCCTCAAGTCCATGCCA GAATGGGGCTCCTGCAAGGACCAGCTCCAGTCCTATATCTGCTTCT GCCTCCCTGCCTTCGAGGGCCGGAACTGTGAGACGCACAAGGATGAC CAGCTGATCTGTGAACGAGAACGGCGGCTGTGAGCAGTACTGCAG TGACCACACGGGCACCAAGCGCTCCTGTCGGTGCCACGAGGGGTACT CTCTGCTGGCAGACGGGGTGTCCTGCACACCCACAGTTGAATATCCA TGTGGAAAAATACCTATTCTAGAAAAAAGAAATGCCAGCAAACCCCA AGGCCGAATTGTGGGGGGCAAGGTGTGCCCCAAAGGGGAGTGTCCA TGGCAGGTCCTGTTGTTGGTGAATGGAGCTCAGTTGTGTGGGGGGAC CCTGATCAACACCATCTGGGTGGTCTCCGCGGCCCACTGTTTCGACAA AATCAAGAACTGGAGGAACCTGATCGCGGTGCTGGGCGAGCACGAC CTCAGCGAGCACGACGGGGATGAGCAGAGCCGGCGGGTGGCGCAGG GCGCTGCTCCGCCTGCACCAGCCCGTGGTCCTCACTGACCATGTGGTG CCCCTCTGCCTGCCCGAACGGACGTTCTCTGAGAGGACGCTGGCCTTC GTGCGCTTCTCATTGGTCAGCGGCTGGGGCCAGCTGCTGGACCGTGG CGCCACGCCCTGGAGCTCATGGTGCTCAACGTGCCCCGGCTGATGA CCCAGGACTGCCTGCAGCAGTCACGGAAGGTGGGAGACTCCCCAAAT ATCACGGAGTACATGTTCTGTGCCGGCTACTCGGATGGCAGCAAGGA CTCCTGCAAGGGGACAGTGGAGGCCCACATGCCACCCACTACCGGG GCACGTGGTACCTGACGGGCATCGTCAGCTGGGGCCAGGGCTGCGCA ACCGTGGGCCACTTTGGGGTGTACACCAGGGTCTCCCAGTACATCGA GTGGCTGCAAAAGCTCATGCGCTCAGAGCCACGCCCAGGAGTCCTCC TGCGAGCCCCATTTCCC

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FIG. 55B

Met Val Ser Gln Ala Leu Arg Leu Leu Cys Leu Leu Leu Gly Leu Gln Gly Cys Leu Ala Ala Val Phe Val Thr Gln Glu Glu Ala His Gly Val Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu lle Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro Lys Gly Glu Cys Pro Trp Gln Val Leu Leu Val Asn Gly Ala Gin Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg Arg Val Ala Gin Val Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn His Asp Ile Ala Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp His Val Val Pro Leu Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr Leu Ala Phe Val Arg Phe Ser Leu Val Ser Gly Trp Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met Val Leu Asn Val Pro Arg Leu Met Thr Gln Asp Cys Leu Gln Gln Ser Arg Lys Val Gly Asp Ser Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala Gly Tyr Ser Asp Gly Ser Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Thr Val Gly His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile Glu Trp Leu Gln Lys Leu Met Arg Ser Glu Pro Arg Pro Gly Val Leu Leu Arg Ala Pro Phe Pro

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FIG. 56A

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAAGCCTCATCAC CATCTGCCTTTTAGGATATCTACTCAGTGCTGAATGTACAGTTTTTCTT GATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAA GTATGGAAGAAAAGTGTAGTTTTGAAGAACCACGAGAAGTTTTTGAA AACACTGAAAAGACAACTGAATTTTGGAAGCAGTATGTTGATGGAGA TCAGTGTGAGTCCAATCCATGTTTAAATGGCGGCAGTTGCAAGGATG ACATTAATTCCTATGAATGTTGGTGTCCCTTTGGATTTGAAGGAAAGA ACTGTGAATTAGATGTAACATGTAACATTAAGAATGGCAGATGCGAG CAGTTTTGTAAAAATAGTGCTGATAACAAGGTGGTTTGCTCCTGTACT GAGGGATATCGACTTGCAGAAAACCAGAAGTCCTGTGAACCAGCAGT GCCATTTCCATGTGGAAGAGTTTCTGTTTCACAAACTTCTAAGCTCAC CCGTGCTGAGGCTGTTTTTCCTGATGTGGACTATGTAAATCCTACTGA AGCTGAAACCATTTTGGATAACATCACTCAAGGCACCCAATCATTTA ATGACTTCACTCGGGTTGTTGGTGGAGAAGATGCCAAACCAGGTCAA TTCCCTTGGCAGGTTGTTTTGAATGGTAAAGTTGATGCATTCTGTGGA GGCTCTATCGTTAATGAAAAATGGATTGTAACTGCTGCCCACTGTGTT GAAACTGGTGTTAAAATTACAGTTGTCGCAGGTGAACATAATATTGA GGAGACAGAACATACAGAGCAAAAGCGAAATGTGATTCGAGCAATT ATTCCTCACCACAACTACAATGCAGCTATTAATAAGTACAACCATGA CATTGCCCTTCTGGAACTGGACGAACCCTTAGTGCTAAACAGCTACG TTACACCTATTTGCATTGCTGACAAGGAATACACGAACATCTTCCTCA AATTTGGATCTGGCTATGTAAGTGGCTGGGCAAGAGTCTTCCACAAA GGGAGATCAGCTTTAGTTCTTCAGTACCTTAGAGTTCCACTTGTTGAC CGAGCCACATGTCTTCGATCTACAAAGTTCACCATCTATAACAACAT GTTCTGTGCTGGCTTCCATGAAGGAGGTAGAGATTCATGTCAAGGAG ATAGTGGGGGACCCCATGTTACTGAAGTGGAAGGGACCAGTTTCTTA ACTGGAATTATTAGCTGGGGTGAAGAGTGTGCAATGAAAGGCAAATA TGGAATATACCAAGGTATCCCGGTATGTCAACTGGATTAAGGAAA AAACAAAGCTCACTTAATGAAAGATGGATTTCCAAGGTTAATTCATT GGAATTGAAAATTAACAG

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FIG. 56B

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Ser Leu Ile Thr Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe LeuAsp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys Met Glu Glu Lys Cys Ser Phe Glu Glu Pro Arg Glu Val Phe Glu Asn Thr Glu Lys Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Ala Val Phe Pro Asp Val Asp Tyr Val Asn Pro Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Gly Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg Ala Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Tro Ala Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr

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FIG. 57A

FIG. 57B

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gin Asp Cys Pro Glu Cys Thr Leu Gin Glu Asn Pro Phe Phe Ser Gin Pro Gly Ala Pro Ile Leu Gin Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro Leu Arg Ser Lys Lys Thr Met Leu Val Gin Lys Asn Val Thr Ser Glu Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr Tyr His Lys Ser

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FIG. 57C

FIG. 57D

Met Lys Thr Leu Gin Phe Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile Cys Cys Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys Ile Gin Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val Ala Thr Gin Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys Glu

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FIG. 58A

CCCGGAGCCGGGCCACCGCGCCCGCTCTGCTCCGACACCGC GCCCCTGGACAGCCGCCTCTCCTCCAGGCCCGTGGGGCTGGCCCT GCACCGCCGAGCTTCCCGGGATGAGGGCCCCCGGTGTGGTCACCCGG CGCGCCCAGGTCGCTGAGGGACCCCGGCCAGGCGCGGAGATGGGG GTGCACGAATGTCCTGCCTGGCTGTGGCTTCTCCTGTCCCTGCTGTCG CTCCCTCTGGGCCTCCCAGTCCTGGGCGCCCCACCACGCCTCATCTGT GACAGCCGAGTCCTGGAGAGGTACCTCTTGGAGGCCAAGGAGGCCG AGAATATCACGACGGGCTGTGCTGAACACTGCAGCTTGAATGAGAAT ATCACTGTCCCAGACACCAAAGTTAATTTCTATGCCTGGAAGAGGAT GGAGGTCGGGCAGCAGGCCGTAGAAGTCTGGCAGGGCCTGGCCCTG CTGTCGGAAGCTGTCCTGCGGGGCCAGGCCCTGTTGGTCAACTCTTCC CAGCCGTGGGAGCCCCTGCAGCTGCATGTGGATAAAGCCGTCAGTGG CCTTCGCAGCCTCACCACTCTGCTTCGGGCTCTGCGAGCCCAGAAGG AAGCCATCTCCCCTCCAGATGCGGCCTCAGCTGCTCCACTCCGAACA ATCACTGCTGACACTTTCCGCAAACTCTTCCGAGTCTACTCCAATTTC CTCCGGGGAAAGCTGAAGCTGTACACAGGGGAGGCCTGCAGGACAG GGGACAGATGACCAGGTGTGTCCACCTGGGCATATCCACCACCTCCC TCACCAACATTGCTTGTGCCACACCCTCCCCGCCACTCCTGAACCCC GTCGAGGGCTCTCAGCTCAGCGCCAGCCTGTCCCATGGACACTCCA GTGCCAGCAATGACATCTCAGGGGCCAGAGGAACTGTCCAGAGAGC AACTCTGAGATCTAAGGATGTCACAGGGCCAACTTGAGGGCCCAGAG CAGGAAGCATTCAGAGAGCAGCTTTAAACTCAGGGACAGAGCCATG CTGGGAAGACGCCTGAGCTCACTCGGCACCCTGCAAAATTTGATGCC AGGACACGCTTTGGAGGCGATTTACCTGTTTTCGCACCTACCATCAGG GACAGGATGACCTGGAGAACTTAGGTGGCAAGCTGTGACTTCTCCAG GTCTCACGGGCATGGGCACTCCCTTGGTGGCAAGAGCCCCCTTGACA CCGGGGTGGTGGGAACCATGAAGACAGGATGGGGGCTGGCCTCTGG CTCTCATGGGGTCCAAGTTTTGTGTATTCTTCAACCTCATTGACAAGA ACTGAAACCACCAAAAAAAAAAAAAA

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FIG. 58B

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp Arg

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FIG. 59A

FIG. 59B

Met Trp Leu Gin Ser Leu Leu Leu Leu Gly Thr Val Ala Cys Ser Ile Ser Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gin Pro Trp Glu His Val Asn Ala Ile Gin Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser Cys Ala Thr Gin Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu

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FIG. 60A

ATGAAATATACAAGTTATATCTTGGCTTTTCAGCTCTGCATCGTTTTG
GGTTCTCTTGGCTGTTACTGCCAGGACCCATATGTAAAAGAAGCAGA
AAACCTTAAGAAATATTTTAATGCAGGTCATTCAGATGTAGCGGATA
ATGGAACTCTTTTCTTAGGCATTTTGAAGAATTGGAAAGAGGAGAGT
GACAGAAAAATAATGCAGAGCCAAATTGTCTCCTTTTACTTCAAACT
TTTTAAAAACTTTAAAGATGACCAGAGCATCCAAAAGAGTGTGGAGA
CCATCAAGGAAGACATGAATGTCAAGTTTTTCAATAGCAACAAAAAG
AAACGAGATGACTTCGAAAAGCTGACTAATTATTCGGTAACTGACTT
GAATGTCCAACGCAAAGCAATACATGAACTCATCCAAGTGATGGCTG
AACTGTCGCCAGCAGCTAAAACAGGAAGCGAAAAAGGAGTCAGAT
GCTGTTTCCGAGGTCGAAGAGCATCCCAGTAA

FIG. 60B

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gin Leu Cys Ile Val Leu Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg Gly Arg Arg Ala Ser Gln

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FIG. 61A

CTGGGACAGTGAATCGACAATGCCGTCTTCTGTCTCGTGGGGCATCCT CCTGCTGGCAGGCCTGTGCTGCCTGGTCCCTGTCTCCCTGGCTGAGGA TCCCCAGGGAGATGCTGCCCAGAAGACAGATACATCCCACCATGATC AGGATCACCCAACCTTCAACAAGATCACCCCCAACCTGGCTGAGTTC GCCTTCAGCCTATACCGCCAGCTGGCACACCAGTCCAACAGCACCAA TATCTTCTCCCCAGTGAGCATCGCTACAGCCTTTGCAATGCTCTC CCTGGGGACCAAGGCTGACACTCACGATGAAATCCTGGAGGGCCTGA ATTTCAACCTCACGGAGATTCCGGAGGCTCAGATCCATGAAGGCTTC GACCACCGGCAATGGCCTGTTCCTCAGCGAGGGCCTGAAGCTAGTGG ATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCAGAAGCCTTC ACTGTCAACTTCGGGGACACCGAAGAGGCCAAGAAACAGATCAACG ATTACGTGGAGAAGGGTACTCAAGGGAAAATTGTGGATTTGGTCAAG GAGCTTGACAGAGACACAGTTTTTGCTCTGGTGAATTACATCTTCTTT AAAGGCAAATGGGAGAGACCCTTTGAAGTCAAGGACACCGAGGAAG AGGACTTCCACGTGGACCAGGTGACCACCGTGAAGGTGCCTATGATG AAGCGTTTAGGCATGTTTAACATCCAGCACTGTAAGAAGCTGTCCAG CTGGGTGCTGCTGATGAAATACCTGGGCAATGCCACCGCCATCTTCT TCCTGCCTGATGAGGGGAAACTACAGCACCTGGAAAATGAACTCACC CACGATATCATCACCAAGTTCCTGGAAAATGAAGACAGAAGGTCTGC CAGCTTACATTTACCCAAACTGTCCATTACTGGAACCTATGATCTGAA GAGCGTCCTGGGTCAACTGGGCATCACTAAGGTCTTCAGCAATGGGG CTGACCTCTCCGGGGTCACAGAGGAGGCACCCCTGAAGCTCTCCAAG GCCGTGCATAAGGCTGTGCTGACCATCGACGAGAAAGGGACTGAAGC TGCTGGGGCCATGTTTTTAGAGGCCATACCCATGTCTATCCCCCCGA GGTCAAGTTCAACAAACCCTTTGTCTTCTTAATGATTGAACAAAATAC AACTGCCTCTCGCTCCTCAACCCCTCCCTCCATCCCTGGCCCCCTCC CTGGATGACATTAAAGAAGGGTTGAGCTGG

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FIG. 61B

Met Pro Ser Ser Val Ser Trp Gly Ile Leu Leu Leu Ala Gly Leu Cys Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gin Leu Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala LeuVal Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu AspArg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gin Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr Gln Lys

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GCTAACCTAGTGCCTATAGCTAAGGCAGGTACCTGCATCCTTGTTTTT GTTTAGTGGATCCTCTATCCTTCAGAGACTCTGGAACCCCTGTGGTCT TCTCTTCATCTAATGACCCTGAGGGGATGGAGTTTTCAAGTCCTTCCA AGCCTCACAGGTTTGCTTCTACTTCAGGCAGTGTCGTGGGCATCAGGT GCCCGCCCTGCATCCCTAAAAGCTTCGGCTACAGCTCGGTGGTGTGT GTCTGCAATGCCACATACTGTGACTCCTTTGACCCCCCGACCTTTCCT GCCCTTGGTACCTTCAGCCGCTATGAGAGTACACGCAGTGGGCGACG GATGGAGCTGAGTATGGGGCCCATCCAGGCTAATCACACGGGCACAG GCCTGCTACTGACCCTGCAGCCAGAACAGAAGTTCCAGAAAGTGAAG GGATTTGGAGGGCCATGACAGATGCTGCTCTCTCAACATCCTTGCC CTGTCACCCCCTGCCCAAAATTTGCTACTTAAATCGTACTTCTCTGAA GAAGGAATCGGATATAACATCATCCGGGTACCCATGGCCAGCTGTGA CTTCTCCATCCGCACCTACACCTATGCAGACACCCCTGATGATTTCCA GTTGCACAACTTCAGCCTCCCAGAGGAAGATACCAAGCTCAAGATAC CCCTGATTCACCGAGCCCTGCAGTTGGCCCAGCGTCCCGTTTCACTCC TTGCCAGCCCCTGGACATCACCCACTTGGCTCAAGACCAATGGAGCG GTGAATGGGAAGGGGTCACTCAAGGGACAGCCCGGAGACATCTACC ACCAGACCTGGGCCAGATACTTTGTGAAGTTCCTGGATGCCTATGCTG AGCACAAGTTACAGTTCTGGGCAGTGACAGCTGAAAATGAGCCTTCT GCTGGGCTGTTGAGTGGATACCCCTTCCAGTGCCTGGGCTTCACCCCT GAACATCAGCGAGACTTCATTGCCCGTGACCTAGGTCCTACCCTCGCC AACAGTACTCACCACAATGTCCGCCTACTCATGCTGGATGACCAACGC TTGCTGCTGCCCCACTGGGCAAAGGTGGTACTGACAGACCCAGAAGC AGCTAAATATGTTCATGGCATTGCTGTACATTGGTACCTGGACTTTCT GGCTCCAGCCAAAGCCACCCTAGGGGAGACACACCGCCTGTTCCCCA ACACCATGCTCTTTGCCTCAGAGGCCTGTGTGGGCTCCAAGTTCTGGG AGCAGAGTGTGCGGCTAGGCTCCTGGGATCGAGGGATGCAGTACAGC CACAGCATCATCACGAACCTCCTGTACCATGTGGTCGGCTGGACCGAC TGGAACCTTGCCCTGAACCCCGAAGGAGGACCCAATTGGGTGCGTAA CTTTGTCGACAGTCCCATCATTGTAGACATCACCAAGGACACGTTTTA CAAACAGCCCATGTTCTACCACCTTGGCCACTTCAGCAAGTTCATTCC TGAGGGCTCCCAGAGAGTGGGGCTGGTTGCCAGTCAGAAGAACGACC TGGACGCAGTGGCACTGATGCATCCCGATGGCTCTGCTGTTGTGGTCG TGCTAAACCGCTCCTCTAAGGATGTGCCTCTTACCATCAAGGATCCTG CTGTGGGCTTCCTGGAGACAATCTCACCTGGCTACTCCATTCACACCT ACCTGTGGCATCGCCAGTGATGGAGCAGATACTCAAGGAGGCACTGG GCTCAGCCTGGGCATTAAAGGGACAGAGTCAGCTCACACGCTGTCTG TGACTAAAGAGGGCACAGCAGGGCCAGTGTGAGCTTACAGCGACGT

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FIG. 62A-2

FIG. 62B

Met Glu Phe Ser Ser Pro Ser Arg Glu Glu Cys Pro Lys Pro Leu Ser Arg Val Ser Ile Met Ala Gly Ser Leu Thr Gly Leu Leu Leu Cln Ala Val Ser Trp Ala Ser Gly Ala Arg Pro Cys Ile Pro Lys Ser Phe Gly Tyr Ser Ser Val Val Cys Val Cys Asn Ala Thr Tyr Cys Asp Ser Phe Asp Pro Pro Thr Phe Pro Ala Leu Gly Thr Phe Ser Arg Tyr Glu Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala Ala Leu Asn Ile Leu Ala Leu Ser Pro Pro Ala Gln Asn Leu Leu Leu Lys Ser Tyr Phe Ser Glu Glu Gly Ile Gly Tyr Asn Ile Ile Arg Val Pro Met Ala Ser Cys Asp Phe Ser Ile Arg Thr Tyr Thr Tyr Ala Asp Thr Pro Asp Asp Phe Gln Leu His Asn Phe Ser Leu Pro Glu Glu Asp Thr Lys Leu Lys Ile Pro Leu Ile His Arg Ala Leu Gln Leu Ala Gln Arg Pro Val Ser Leu Leu Ala Ser Pro Trp Thr Ser Pro Thr Trp Leu Lys Thr Asn Gly Ala Val Asn Gly Lys Gly Ser Leu Lys Gly Gln Pro Gly Asp Ile Tyr His Gln Thr Trp Ala Arg Tyr Phe Val Lys Phe Leu Asp Ala Tyr Ala Glu His Lys Leu Gln Phe Trp Ala Val Thr Ala Glu Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu Gly Phe Thr Pro Glu His Gln Arg Asp Phe Ile Ala Arg Asp Leu Gly Pro Thr Leu Ala Asn Ser Thr His His Asn Val Arg Leu Leu Met Leu Asp Asp Gln Arg Leu Leu Leu Pro His Trp Ala Lys Val Val Leu Thr Asp Pro Glu Ala Ala Lys Tyr Val His Gly Ile Ala Val His Trp Tyr Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp Thr Phe Tyr Lys Gln Pro Met Phe Tyr His Leu Gly His Phe Ser Lys Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val Val Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys Asp Pro Ala Val Gly Phe Leu Glu Thr Ile Ser Pro Gly Tyr Ser Ile His Thr Tyr Leu Trp His Arg Gln

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ATGGATGCAATGAAGAGAGGGCTCTGCTGTGTGCTGCTGTGTGG AGCAGTCTTCGTTTCGCCCAGCCAGGAAATCCATGCCCGATTCAGAA GAGGAGCCAGATCTTACCAAGTGATCTGCAGAGATGAAAAAACGCA GATGATATACCAGCAACATCAGTCATGGCTGCGCCCTGTGCTCAGAA GCAACCGGGTGGAATATTGCTGGTGCAACAGTGGCAGGGCACAGTGC CACTCAGTGCCTGTCAAAAGTTGCAGCGAGCCAAGGTGTTTCAACGG GGGCACCTGCCAGCAGGCCCTGTACTTCTCAGATTTCGTGTGCCAGTG CCCCGAAGGATTTGCTGGGAAGTGCTGTGAAATAGATACCAGGGCCA CGTGCTACGAGGACCAGGGCATCAGCTACAGGGGCACGTGGAGCAC AGCGGAGAGTGGCGCCGAGTGCACCAACTGGAACAGCAGCGCGTTG GCCCAGAAGCCCTACAGCGGGCGGAGGCCAGACGCCATCAGGCTGG GCCTGGGGAACCACAACTACTGCAGAAACCCAGATCGAGACTCAAA GCCCTGGTGCTACGTCTTTAAGGCGGGGAAGTACAGCTCAGAGTTCT GCAGCACCCCTGCCTGCTCTGAGGGAAACAGTGACTGCTACTTTGGG AATGGGTCAGCCTACCGTGGCACGCACAGCCTCACCGAGTCGGGTGC CTCCTGCCTCCGTGGAATTCCATGATCCTGATAGGCAAGGTTTACAC AGCACAGAACCCCAGTGCCCAGGCACTGGGCCTGGGCAAACATAATT ACTGCCGGAATCCTGATGGGGATGCCAAGCCCTGGTGCCACGTGCTG AAGAACCGCAGGCTGACGTGGGAGTACTGTGATGTGCCCTCCTGCTC CACCTGCGGCCTGAGACAGTACAGCCAGCCTCAGTTTCGCATCAAAG GAGGGCTCTTCGCCGACATCGCCTCCCACCCCTGGCAGGCTGCCATCT TTGCCAAGCACAGGAGGTCGCCGGGAGAGCGGTTCCTGTGCGGGGGC ATACTCATCAGCTCCTGCTGGATTCTCTCTGCCGCCCACTGCTTCCAG GAGAGGTTTCCGCCCCACCACCTGACGGTGATCTTGGGCAGAACATA CCGGGTGGTCCCTGGCGAGGAGGAGCAGAAATTTGAAGTCGAAAAA TACATTGTCCATAAGGAATTCGATGATGACACTTACGACAATGACAT TGCGCTGCTGCAGCTGAAATCGGATTCGTCCCGCTGTGCCCAGGAGA GCAGCGTGGTCCGCACTGTGTGCCTTCCCCCGGCGGACCTGCAGCTG CCGGACTGGACGGAGTGTGAGCTCTCCGGCTACGGCAAGCATGAGGC CTTGTCTCCTTTCTATTCGGAGCGGCTGAAGGAGGCTCATGTCAGACT GTACCCATCCAGCCGCTGCACATCACAACATTTACTTAACAGAACAG TCACCGACAACATGCTGTGTGCTGGAGACACTCGGAGCGGCGGGCCC CAGGCAÁACTTGCACGACGCCTGCCAGGGCGATTCGGGAGGCCCCCT GGTGTGTCTGAACGATGGCCGCATGACTTTGGTGGGCATCATCAGCT GGGGCCTGGGCTGTGGACAGAAGGATGTCCCGGGTGTGTACACCAAG GTTACCAACTACCTAGACTGGATTCGTGACAACATGCGACCGTGACC AGGAACACCCGACTCCTCAAAAGCAAATGAGATCC

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FIG. 63B

Met Asp Ala Met Lys Arg Gly Leu Cys Cys Val Leu Leu Leu Cys Gly Ala Val Phe Val Ser Pro Ser Gln Glu Ile His Ala Arg Phe Arg Arg Gly Ala Arg Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gin Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gin Ala Asn Leu His Asp Ala Cys Gin Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met

259/345 FIG. 64A

ATCACTCTCTTTAATCACTACTCACATTAACCTCAACTCCTGCCACAA TGTACAGGATGCAACTCCTGTCTTGCATTGCACTAATTCTTGCACTTG TCACAAACAGTGCACCTACTTCAAGTTCGACAAAGAAAACAAAGAAA ACACAGCTACAACTGGAGCATTTACTGCTGGATTTACAGATGATTTTG AATGGAATTAATAATTACAAGAATCCCAAACTCACCAGGATGCTCAC ATTTAAGTTTTACATGCCCAAGAAGGCCACAGAACTGAAACAGCTTC AGTGTCTAGAAGAAGAACTCAAACCTCTGGAGGAAGTGCTGAATTTA GCTCAAAGCAAAAACTTTCACTTAAGACCCAGGGACTTAATCAGCAA TATCAACGTAATAGTTCTGGAACTAAAGGGATCTGAAACAACATTCA TGTGTGAATATGCAGATGAGACAGCAACCATTGTAGAATTTCTGAAC AGATGGATTACCTTTTGTCAAAGCATCATCTCAACACTAACTTGATAA AATATTTAAATTTTATATTTATTGTTGAATGTATGGTTGCTACCTATTG TAACTATTATTCTTAATCTTAAAACTATAAATATGGATCTTTTATGAT CAAAAATATTTATTATTATGTTGAATGTTAAATATAGTATCTATGTAG AAACAAAAAAAAAA

FIG. 64B

Met Tyr Arg Met Gin Leu Leu Ser Cys Ile Ala Leu Ile Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys Gin Leu Gln Cys Leu Glu Glu Ual Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr

260/345 FIG. 65A-1

ATGCAAATAGAGCTCTCCACCTGCTTCTTTCTGTGCCTTTTGCGATTCT GCTTTAGTGCCACCAGAAGATACTACCTGGGTGCAGTGGAACTGTCA TGGGACTATATGCAAAGTGATCTCGGTGAGCTGCCTGTGGACGCAAG ATTTCCTCCTAGAGTGCCAAAATCTTTTCCATTCAACACCTCAGTCGT GTACAAAAGACTCTGTTTGTAGAATTCACGGATCACCTTTTCAACAT CGCTAAGCCAAGGCCACCCTGGATGGGTCTGCTAGGTCCTACCATCC AGGCTGAGGTTTATGATACAGTGGTCATTACACTTAAGAACATGGCT TCCCATCCTGTCAGTCTTCATGCTGTTGGTGTATCCTACTGGAAAGCT TCTGAGGGAGCTGAATATGATGATCAGACCAGTCAAAGGGAGAAAG AAGATGATAAAGTCTTCCCTGGTGGAAGCCATACATATGTCTGGCAG GTCCTGAAAGAGAATGGTCCAATGGCCTCTGACCCACTGTGCCTTAC CTACTCATATCTTCTCATGTGGACCTGGTAAAAGACTTGAATTCAGG CCTCATTGGAGCCCTACTAGTATGTAGAGAAGGGAGTCTGGCCAAGG AAAAGACACAGACCTTGCACAAATTTATACTACTTTTTGCTGTATTTG ATGAAGGGAAAAGTTGGCACTCAGAAACAAAGAACTCCTTGATGCA GGATAGGGATGCTGCATCTGCTCGGGCCTGGCCTAAAATGCACACAG TCAATGGTTATGTAAACAGGTCTCTGCCAGGTCTGATTGGATGCCACA GGAAATCAGTCTATTGGCATGTGATTGGAATGGGCACCACTCCTGAA GTGCACTCAATATTCCTCGAAGGTCACACATTTCTTGTGAGGAACCAT CGCCAGGCGTCCTTGGAAATCTCGCCAATAACTTTCCTTACTGCTCAA ACACTCTTGATGGACCTTGGACAGTTTCTACTGTTTTGTCATATCTCTT CCCACCAACATGATGGCATGGAAGCTTATGTCAAAGTAGACAGCTGT CCAGAGGAACCCCAACTACGAATGAAAAATAATGAAGAAGCGGAAG ACTATGATGATGATCTTACTGATTCTGAAATGGATGTGGTCAGGTTTG ATGATGACAACTCTCCTTCCTTTATCCAAATTCGCTCAGTTGCCAAGA AGCATCCTAAAACTTGGGTACATTACATTGCTGCTGAAGAGGAGGAC TGGGACTATGCTCCCTTAGTCCTCGCCCCCGATGACAGAAGTTATAAA AGTCAATATTTGAACAATGGCCCTCAGCGGATTGGTAGGAAGTACAA AAAAGTCCGATTTATGGCATACACAGATGAAACCTTTAAGACTCGTG AAGCTATTCAGCATGAATCAGGAATCTTGGGACCTTTACTTTATGGGG TCAAGGAGATTACCAAAAGGTGTAAAACATTTGAAGGATTTTCCAAT TCTGCCAGGAGAATATTCAAATATAAATGGACAGTGACTGTAGAAG ATGGGCCAACTAAATCAGATCCTCGGTGCCTGACCCGCTATTACTCTA GTTTCGTTAATATGGAGAGAGATCTAGCTTCAGGACTCATTGGCCCTC TCCTCATCTGCTACAAAGAATCTGTAGATCAAAGAGGAAACCAGATA ATGTCAGACAAGAGGAATGTCATCCTGTTTTCTGTATTTGATGAGAAC CGAAGCTGGTACCTCACAGAGAATATACAACGCTTTCTCCCCAATCCA GCTGGAGTGCAGCTTGAGGATCCAGAGTTCCAAGCCTCCAACATCAT GCACAGCATCAATGGCTATGTTTTTGATAGTTTGCAGTTGTCAGTTTG TTTGCATGAGGTGGCATACTGGTACATTCTAAGCATTGGAGCACAGA CTGACTTCCTTCTGTCTTCTCTGGATATACCTTCAAACACAAAAT

261/345 FIG. 65A-2

GGTCTATGAAGACACACTCACCCTATTCCCATTCTCAGGAGAAACTGT CTTCATGTCGATGGAAAACCCAGGTCTATGGATTCTGGGGTGCCACA ACTCAGACTTTCGGAACAGAGGCATGACCGCCTTACTGAAGGTTTCT AGTTGTGACAAGAACACTGGTGATTATTACGAGGACAGTTATGAAGA TATTTCAGCATACTTGCTGAGTAAAAACAATGCCATTGAACCAAGAA GCTTCTCCCAGAATTCAAGACACCGTAGCACTAGGCAAAAGCAATTT AATGCCACCACAATTCCAGAAAATGACATAGAGAAGACTGACCCTTG GTTTGCACACAGAACACCTATGCCTAAAATACAAAATGTCTCCTCTA GTGATTTGTTGATGCTCTTGCGACAGAGTCCTACTCCACATGGGCTAT CCTTATCTGATCTCCAAGAAGCCAAATATGAGACTTTTTCTGATGATC CATCACCTGGAGCAATAGACAGTAATAACAGCCTGTCTGAAATGACA CACTTCAGGCCACAGCTCCATCACAGTGGGGACATGGTATTTACCCC TGAGTCAGGCCTCCAATTAAGATTAAATGAGAAACTGGGGACAACTG CAGCAACAGAGTTGAAGAAACTTGATTTCAAAGTTTCTAGTACATCA AATAATCTGATTTCAACAATTCCATCAGACAATTTGGCAGCAGGTACT GATAATACAAGTTCCTTAGGACCCCCAAGTATGCCAGTTCATTATGAT AGTCAATTAGATACCACTCTATTTGGCAAAAAGTCATCTCCCCTTACT GAGTCTGGTGGACCTCTGAGCTTGAGTGAAGAAAATAATGATTCAAA GTTGTTAGAATCAGGTTTAATGAATAGCCAAGAAAGTTCATGGGGAA AAAATGTATCGTCAACAGAGAGTGGTAGGTTATTTAAAGGGAAAAGA GCTCATGGACCTGCTTTGTTGACTAAAGATAATGCCTTATTCAAAGTT AGCATCTCTTTGTTAAAGACAAACAAAACTTCCAATAATTCAGCAACT AATAGAAAGACTCACATTGATGGCCCATCATTATTAATTGAGAATAG TCCATCAGTCTGGCAAAATATATTAGAAAGTGACACTGAGTTTAAAA AAGTGACACCTTTGATTCATGACAGAATGCTTATGGACAAAAATGCT ACAGCTTTGAGGCTAAATCATATGTCAAATAAAACTACTTCATCAAA AAACATGGAAATGGTCCAACAGAAAAAAGAGGGCCCCATTCCACCA GATGCACAAAATCCAGATATGTCGTTCTTTAAGATGCTATTCTTGCCA GAATCAGCAAGGTGGATACAAAGGACTCATGGAAAGAACTCTCTGAA CTCTGGGCAAGGCCCCAGTCCAAAGCAATTAGTATCCTTAGGACCAG AAAAATCTGTGGAAGGTCAGAATTTCTTGTCTGAGAAAAAACAAAGTG GTAGTAGGAAAGGGTGAATTTACAAAGGACGTAGGACTCAAAGAGA TGGTTTTTCCAAGCAGCAGAAACCTATTTCTTACTAACTTGGATAATT TACATGAAAATAATACACACAATCAAGAAAAAAAAAATTCAGGAAGA AATAGAAAAGAAGGAAACATTAATCCAAGAGAATGTAGTTTTGCCTC AGATACATACAGTGACTGGCACTAAGAATTTCATGAAGAACCTTTTC TTACTGAGCACTAGGCAAAATGTAGAAGGTTCATATGACGGGGCATA TGCTCCAGTACTTCAAGATTTTAGGTCATTAAATGATTCAACAAATAG AACAAAGAAACACACAGCTCATTTCTCAAAAAAAGGGGAGGAAGAA AACTTGGAAGGCTTGGGAAATCAAACCAGCAAATTGTAGAGAAATAT GCATGCACCACAAGGAATATCTCCTAATACAAGCCAGCAGAATTTTG TCACGCAACGTAGTAAGAGAGCTTTGAAACAATTCAGACTCCCACTA

262/345 FIG. 65A-3

GAAGAACAGAACTTGAAAAAAGGATAATTGTGGATGACACCTCAAC CCAGTGGTCCAAAAACATGAAACATTTGACCCCGAGCACCCTCACAC AGATAGACTACAATGAGAAGGAGAAAGGGGCCATTACTCAGTCTCCC TTATCAGATTGCCTTACGAGGAGTCATAGCATCCCTCAAGCAAATAGA TCTCCATTACCCATTGCAAAGGTATCATCATTTCCATCTATTAGACCTA TATATCTGACCAGGGTCCTATTCCAAGACAACTCTTCTCATCTTCCAG CAGCATCTTATAGAAAGAAAGATTCTGGGGTCCAAGAAAGCAGTCAT TTCTTACAAGGAGCCAAAAAAAAAAACCTTTCTTTAGCCATTCTAACC TTGGAGATGACTGGTGATCAAAGAGAGGTTGGCTCCCTGGGGACAAG TGCCACAAATTCAGTCACATACAAGAAAGTTGAGAACACTGTTCTCCC GAAACCAGACTTGCCCAAAACATCTGGCAAAGTTGAATTGCTTCCAA AAGTTCACATTTATCAGAAGGACCTATTCCCTACGGAAACTAGCAATG GGTCTCCTGGCCATCTGGATCTCGTGGAAGGGAGCCTTCTTCAGGGAA CAGAGGGAGCGATTAAGTGGAATGAAGCAAACAGACCTGGAAAAGT GCTATTGGATCCTCTTGCTTGGGATAACCACTATGGTACTCAGATACC AAAAGAAGAGTGGAAATCCCAAGAGAAGTCACCAGAAAAAACAGCT TTTAAGAAAAAGGATACCATTTTGTCCCTGAACGCTTGTGAAAGCAAT CATGCAATAGCAGCAATAAATGAGGGACAAAATAAGCCCGAAATAG AAGTCACCTGGGCAAAGCAAGGTAGGACTGAAAGGCTGTGCTCTCAA AACCCACCAGTCTTGAAACGCCATCAACGGGAAATAACTCGTACTAC TCTTCAGTCAGATCAAGAGGAAATTGACTATGATGATACCATATCAGT TGAAATGAAGAAGGAAGATTTTGACATTTATGATGAGGATGAAAATC AGAGCCCCCGCAGCTTTCAAAAGAAAACACGACACTATTTTATTGCTG CAGTGGAGAGGCTCTGGGATTATGGGATGAGTAGCTCCCCACATGTT CTAAGAAACAGGGCTCAGAGTGGCAGTGTCCCTCAGTTCAAGAAAGT TGTTTTCCAGGAATTTACTGATGGCTCCTTTACTCAGCCCTTATACCGT GGAGAACTAAATGAACATTTGGGACTCCTGGGGCCATATATAAGAGC AGAAGTTGAAGATAATATCATGGTAACTTTCAGAAATCAGGCCTCTC GTCCCTATTCCTATTCTAGCCTTATTTCTTATGAGGAAGATCAGAG GCAAGGAGCAGAACCTAGAAAAAACTTTGTCAAGCCTAATGAAACCA AAACTTACTTTTGGAAAGTGCAACATCATATGGCACCCACTAAAGAT GAGTTTGACTGCAAAGCCTGGGCTTATTTCTCTGATGTTGACCTGGAA AAAGATGTGCACTCAGGCCTGATTGGACCCCTTCTGGTCTGCCACACT AACACACTGAACCCTGCTCATGGGAGACAAGTGACAGTACAGGAATT TGCTCTGTTTTTCACCATCTTTGATGAGACCAAAAGCTGGTACTTCACT GAAAATATGGAAAGAAACTGCAGGGCTCCCTGCAATATCCAGATGGA CATAATGGATACACTACCTGGCTTAGTAATGGCTCAGGATCAAAGGA TTCGATGGTATCTGCTCAGCATGGGCAGCAATGAAAACATCCATTCT TAAAATGGCACTGTACAATCTCTATCCAGGTGTTTTTTGAGACAGTGGA

263/345 FIG. 65A-4

AATGTTACCATCCAAAGCTGGAATTTGGCGGGTGGAATGCCTTATTGG CGAGCATCTACATGCTGGGATGAGCACACTTTTTCTGGTGTACAGCAA TAAGTGTCAGACTCCCCTGGGAATGGCTTCTGGACACATTAGAGATTT TCAGATTACAGCTTCAGGACAATATGGACAGTGGGCCCCAAAGCTGG CCAGACTTCATTATTCCGGATCAATCAATGCCTGGAGCACCAAGGAG CCCTTTCTTGGATCAAGGTGGATCTGTTGGCACCAATGATTATTCAC GGCATCAAGACCCAGGGTGCCCGTCAGAAGTTCTCCAGCCTCTACAT CTCTCAGTTTATCATCATGTATAGTCTTGATGGGAAGAAGTGGCAGA CTTATCGAGGAAATTCCACTGGAACCTTAATGGTCTTCTTTGGCAATG TGGATTCATCTGGGATAAAACACAATATTTTTAACCCTCCAATTATTG CTCGATACATCCGTTTGCACCCAACTCATTATAGCATTCGCAGCACTC TTCGCATGGAGTTGATGGGCTGTGATTTAAATAGTTGCAGCATGCCAT TGGGAATGGAGAGTAAAGCAATATCAGATGCACAGATTACTGCTTCA TCCTACTTTACCAATATGTTTGCCACCTGGTCTCCTTCAAAAGCTCGA CTTCACCTCCAAGGGAGGAGTAATGCCTGGAGACCTCAGGTGAATAA TCCAAAAGAGTGGCTGCAAGTGGACTTCCAGAAGACAATGAAAGTCA CAGGAGTAACTACTCAGGGAGTAAAATCTCTGCTTACCAGCATGTAT GTGAAGGAGTTCCTCATCTCCAGCAGTCAAGATGGCCATCAGTGGAC TCTCTTTTTCAGAATGGCAAAGTAAAGGTTTTTCAGGGAAATCAAGA CTCCTTCACACCTGTGGTGAACTCTCTAGACCCACCGTTACTGACTCG CTACCTTCGAATTCACCCCCAGAGTTGGGTGCACCAGATTGCCCTGAG GATGGAGGTTCTGGGCTGCGAGGCACAGGACCTCTACTGAGGGTGGC CACTGCAGCACCTGCCACTGCCGTCACCTCTCCCTCCTCAGCTCCAGG GCAGTGTCCCTCCCTGGCTTGCCTTCTACCTTTGTGCTAAATCCTAGC AGACACTGCCTTGAAGCCTCCTGAATTAACTATCATCAGTCCTGCATT TCTTTGGTGGGGGCCAGGAGGGTGCATCCAATTTAACTTAACTCTTA AGGCAAAAAGAAGTGAGGAGAAACCTGCATGAAAGCATTCTTCCCTG AAAAGTTAGGCCTCTCAGAGTCACCACTTCCTCTGTTGTAGAAAAACT ATGTGATGAAACTTTGAAAAAGATATTTATGATGTTAACATTTCAGGT TAAGCCTCATACGTTTAAAATAAAACTCTCAGTTGTTTATTATCCTGA TCAAGCATGGAACAAAGCATGTTTCAGGATCAGATCAATACAATCTT GGAGTCAAAAGGCAAATCATTTGGACAATCTGCAAAATGGAGAGAA TACAATAACTACTACAGTAAAGTCTGTTTCTGCTTCCTTACACATAGA TATAATTATGTTATTTAGTCATTATGAGGGGCACATTCTTATCTCCAA AACTAGCATTCTTAAACTGAGAATTATAGATGGGGTTCAAGAATCCC TAAGTCCCCTGAAATTATATAAGGCATTCTGTATAAATGCAAATGTGC ATTTTTCTGACGAGTGTCCATAGATATAAAGCCATTTGGTCTTAATTCT GACCAATAAAAAAATAAGTCAGGAGGATGCAATTGTTGAAAGCTTTG AAATGATGA

264/345 FIG. 65B-1

Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met Ĝlu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asp Ser Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Île Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp Ile Glu Lys Thr Asp Pro Trp

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Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gin Ser Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu Ser Ser Trp Gly Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala Leu Phe Lys Val Ser Ile Ser Leu Leu Lys Thr Asn Lys Thr Ser Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp Gly Pro Ser Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu Ser Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg Met Leu Met Asp Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met Ser Asn Lys Thr Thr Ser Ser Lys Asn Met Glu Met Val Gln Gln Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala Gln Asn Pro Asp Met Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro Ser Pro Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu Gly Gln Asn Phe Leu Ser Glu Lys Asn Lys Val Val Val Gly Lys Gly Glu Phe Thr Lys Asp Val Gly Leu Lys Glu Met Val Phe Pro Ser Ser Arg Asn Leu Phe Leu Thr Asn Leu Asp Asn Leu His Glu Asn Asn Thr His Asn Gln Glu Lys Lys Ile Gln Glu Glu Ile Glu Lys Lys Glu Thr Leu Ile Gln Glu Asn Val Val Leu Pro Gln Ile His Thr Val Thr Gly Thr Lys Asn Phe Met Lys Asn Leu Phe Leu Leu Ser Thr Arg Gln Asn Val Glu Gly Ser Tyr Asp Gly Ala Tyr Ala Pro Val Leu Gln Asp Phe Arg Ser Leu Asn Asp Ser Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys Lys Gly Glu Glu Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val Glu Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn Phe Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro Leu Glu Glu Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser Thr Gln Trp Ser Lys Asn Met Lys His Leu Thr Pro Ser Thr Leu Thr Gln Ile Asp Tyr Asn Glu Lys Glu Lys Gly Ala Ile Thr Gln Ser Pro Leu Ser Asp Cys Leu Thr Arg Ser His Ser Ile Pro Gln Ala Asn Arg Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile Arg Pro Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro Ala Ala Ser Tyr Arg Lys Lys Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu Gln Gly Ala Lys Lys Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr Gly Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys Val His Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu

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Leu Gln Gly Thr Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys Val Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser Lys Leu Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys Thr Ala Phe Lys Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly Gln Asn Lys Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr Glu Arg Leu Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asp Glu Asp Glu Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr Leu Arg Ile His

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Pro Gl
n Ser Trp Val His Gl
n Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gl
n Asp Leu Tyr

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FIG. 66A

TCCACCTGTCCCGCAGCGCCGGCTCGCGCCCTCCTGCCGCAGCCACC GAGCCGCCGTCTAGCGCCCCGACCTCGCCACCATGAGAGCCCTGCTG GCGCGCCTGCTTCTCTGCGTCCTGGTCGTGAGCGACTCCAAAGGCAGC AATGAACTTCATCAAGTTCCATCGAACTGTGACTGTCTAAATGGAGGA ACATGTGTGTCCAACAAGTACTTCTCCAACATTCACTGGTGCAACTGC CCAAAGAAATTCGGAGGGCAGCACTGTGAAATAGATAAGTCAAAAAC CTGCTATGAGGGGAATGGTCACTTTTACCGAGGAAAGGCCAGCACTG ACACCATGGGCCGGCCCTGCCTGCCTGGAACTCTGCCACTGTCCTTC AGCAAACGTACCATGCCCACAGATCTGATGCTCTTCAGCTGGGCCTGG GGAAACATAATTACTGCAGGAACCCAGACAACCGGAGGCGACCCTGG TGCTATGTGCAGGTGGGCCTAAAGCCGCTTGTCCAAGAGTGCATGGT GCATGACTGCGCAGATGGAAAAAAGCCCTCCTCCTCCAGAAGAAT TAAAATTTCAGTGTGGCCAAAAGACTCTGAGGCCCCGCTTTAAGATTA TTGGGGGAGAATTCACCACCATCGAGAACCAGCCCTGGTTTGCGGCC ATCTACAGGAGGCACCGGGGGGGCTCTGTCACCTACGTGTGGGAGG CAGCCTCATCAGCCCTTGCTGGGTGATCAGCGCCACACACTGCTTCAT TGATTACCCAAAGAAGGAGGACTACATCGTCTACCTGGGTCGCTCAA GGCTTAACTCCAACACGCAAGGGGAGATGAAGTTTGAGGTGGAAAAC CTCATCCTACACAAGGACTACAGCGCTGACACGCTTGCTCACCACAAC GACATTGCCTTGCTGAAGATCCGTTCCAAGGAGGGCAGGTGTGCGCA GCCATCCGGACTATACAGACCATCTGCCTGCCCTCGATGTATAACGA TCCCCAGTTTGGCACAAGCTGTGAGATCACTGGCTTTGGAAAAGAGA ATTCTACCGACTATCTCTATCCGGAGCAGCTGAAGATGACTGTTGTGA AGCTGATTTCCCACCGGGAGTGTCAGCAGCCCCACTACTACGGCTCTG AAGTCACCACCAAAATGCTGTGTGCTGCTGACCCACAGTGGAAAACA GATTCCTGCCAGGGAGACTCAGGGGGACCCCTCGTCTGTTCCCTCCAA GGCCGCATGACTTTGACTGGAATTGTGAGCTGGGGCCGTGGATGTGC CCTGAAGGACAAGCCAGGCGTCTACACGAGAGTCTCACACTTCTTAC GGGTCCCCAGGGAGGAAACGGGCACCACCCGCTTTCTTGCTGGTTGTC ATTTTTGCAGTAGAGTCATCTCCATCAGCTGTAAGAAGAGACTGGGA AGAT

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FIG. 66B

Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Tro Asn Ser Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Glv Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Gin Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

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FIG.67A

TCCTGCACAGGCAGTGCCTTGAAGTGCTTCTTCAGAGACCTTTCTTCA TAGACTACTTTTTTTTTTTAAGCAGCAAAAGGAGAAAATTGTCATCA AGGATATTCCAGATTCTTGACAGCATTCTCGTCATCTCTGAGGACATC ACCATCATCTCAGGATGAGGGGCATGAAGCTGCTGGGGGCGCTGCTG GCACTGGCGGCCCTACTGCAGGGGGCCGTGTCCCTGAAGATCGCAGC CTTCAACATCCAGACATTTGGGGAGACCAAGATGTCCAATGCCACCCT CGTCAGCTACATTGTGCAGATCCTGAGCCGCTATGACATCGCCCTGGT CCAGGAGGTCAGAGACAGCCACCTGACTGCCGTGGGGAAGCTGCTGG ACAACCTCAATCAGGATGCACCAGACACCTATCACTACGTGGTCAGT GAGCCACTGGGACGGAACAGCTATAAGGAGCGCTACCTGTTCGTGTA CAGGCCTGACCAGGTGTCTGCGGTGGACAGCTACTACTACGATGATG GTCAGGTTCTTCTCCCGGTTCACAGAGGTCAGGGAGTTTGCCATTGTT CCCCTGCATGCGGCCCCGGGGGACGCAGTAGCCGAGATCGACGCTCT CTATGACGTCTACCTGGATGTCCAAGAGAAATGGGGCTTGGAGGACG TCATGTTGATGGGCGACTTCAATGCGGGCTGCAGCTATGTGAGACCCT CCCAGTGGTCATCCATCCGCCTGTGGACAAGCCCCACCTTCCAGTGGC TGATCCCCGACAGCGCTGACACCACAGCTACACCCACGCACTGTGCCT ATGACAGGATCGTGGTTGCAGGGATGCTGCTCCGAGGCGCCGTTGTTC CCGACTCGGCTCTTCCCTTTAACTTCCAGGCTGCCTATGGCCTGAGTG ACCAACTGGCCCAAGCCATCAGTGACCACTATCCAGTGGAGGTGATG CTGAAGTGAGCAGCCCCTCCCCACACCAGTTGAACTGCAG

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FIG. 67B

Met Arg Gly Met Lys Leu Leu Gly Ala Leu Leu Ala Leu Ala Ala Leu Leu Gln Gly Ala Val Ser Leu Lys Ile Ala Ala Phe Asn Ile Gln Thr Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn Ala Gly Cys Ser Tyr Val Arg Pro Ser Gln Trp Ser Ser Ile Arg Leu Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Val Ala Gly Met Leu Leu Arg Gly Ala Val Val Pro Asp Ser Ala Leu Pro Phe Asn Phe Gln Ala Ala Tyr Gly Leu Ser Asp Gln Leu Ala Gln Ala Ile Ser Asp His Tyr Pro Val Glu Val Met Leu Lys

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FIG. 68A

FIG. 68B

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu Trp Gly Pro Asp Pro Ala Ala Ala Phe Val Asn Glm His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Glm Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn

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FIG. 69A

ATGGGAGGTTGGTCTTCCAAACCTCGACAAGGCATGGGGACGAATCT TTCTGTTCCCAATCCTCTGGGATTCTTTCCCGATCACCAGTTGGACCCT GCGTTCGGAGCCAACTCAAACAATCCAGATTGGGACTTCAACCCCAA CAAGGATCACTGGCCAGAGGCAATCAAGGTAGGAGCGGGAGACTTC GGGCCAGGGTTCACCCCACCACACGGCGGTCTTTTGGGGTGGAGCCC TCAGGCTCAGGGCATATTGACAACAGTGCCAGCAGCGCCTCCTCCTG TTTCCACCAATCGGCAGTCAGGAAGACAGCCTACTCCCATCTCTCCAC CTCTAAGAGACAGTCATCCTCAGGCCATGCAGTGGAACTCCACAACA TTCCACCAAGCTCTGCTAGATCCCAGAGTGAGGGGCCTATATTTTCCT GCTGGTGGCTCCAGTTCCGGAACAGTAAACCCTGTTCCGACTACTGTC TCACCCATATCGTCAATCTTCTCGAGGACTGGGGACCCTGCACCGAAC ATGGAGAGCACAACATCAGGATTCCTAGGACCCCTGCTCGTGTTACA GGCGGGGTTTTTCTTGTTGACAAGAATCCTCACAATACCACAGAGTCT AGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGAGCACCCACGTG TTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTT ATCATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTC TTCTGGACTACCAAGGTATGTTGCCCGTTTGTCCTCTACTTCCAGGAA CATCAACTACCAGCACGGGACCATGCAAGACCTGCACGATTCCTGCT CAAGGAACCTCTATGTTTCCCTCTTGTTGCTGTACAAAACCTTCGGAC GGAAACTGCACTTGTATTCCCATCCCATCATCCTGGGCTTTCGCAAGA TTCCTATGGGAGTGGGCCTCAGTCCGTTTCTCCTGGCTCAGTTTACTA GTGCCATTTGTTCAGTGGTTCGCAGGGCTTTCCCCCACTGTTTGGCTTT CAGTTATATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAACATCT TGAGTCCCTTTTTACCTCTATTACCAATTTTCTTTTGTCTTTGGGTATAC ATTTGA

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FIG. 69B

Met Gly Gly Trp Ser Ser Lys Pro Arg Gln Gly Met Gly Thr Asn Leu Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn Lys Asp His Trp Pro Glu Ala Ile Lys Val Gly Ala Gly Asp Phe Gly Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Val Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser Pro Ile Ser Ser Ile Phe Ser Arg Thr Gly Asp Pro Ala Pro Asn Met Glu Ser Thr Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Ile Pro Ala Gln Gly Thr Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Ala Gly Leu Ser Pro Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile

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FIG. 70A

CGAACCACTCAGGGTCCTGTGGACAGCTCACCTAGCTGCAATGGCTA CCTGGCTTCAAGAGGGCAGTGCCTTCCCAACCATTCCCTTATCCAGGC CTTTTGACAACGCTATGCTCCGCGCCCATCGTCTGCACCAGCTGGCCT TTGACACCTACCAGGAGTTTGAAGAAGCCTATATCCCAAAGGAACAG AAGTATTCATTCCTGCAGAACCCCCAGACCTCCCTCTGTTTCTCAGAG TCTATTCCGACACCCTCCAACAGGGAGGAAACACAACAGAAATCCAA CCTAGAGCTGCTCCGCATCTCCCTGCTGCTCATCCAGTCGTGGCTGGA GCCCGTGCAGTTCCTCAGGAGTGTCTTCGCCAACAGCCTGGTGTACGG CGCCTCTGACAGCAACGTCTATGACCTCCTAAAGGACCTAGAGGAAG GCATCCAAACGCTGATGGGGAGGCTGGAAGATGGCAGCCCCCGGACT GGGCAGATCTTCAAGCAGACCTACAGCAAGTTCGACACAAACTCACA CAACGATGACGCACTACTCAAGAACTACGGGCTGCTCTACTGCTTCAG GAAGGACATGGCAAGGTCGAGACATTCCTGCGCATCGTGCAGTGCCG CTCTGTGGAGGGCAGCTGTGGCTTCTAGCTGCCCGGGTGGCATCCCTG TGACCCCTCCCCAGTGCCTCTCCTGGCCCTGGAAGTTGCCACTCCAGT GCCCACCAGCCTTGTCCTAATAAAATTAAGTTGCATC

FIG. 70B

Met Ala Thr Gly Ser Arg Thr Ser Leu Leu Leu Ala Phe Gly Leu Leu Cys Leu Pro Trp Leu Gln Glu Gly Ser Ala Phe Pro Thr Ile Pro Leu Ser Arg Pro Phe Asp Asn Ala Met Leu Arg Ala His Arg Leu His Gln Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg Glu Glu Thr Gln Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu Leu Leu Ile Gln Ser Trp Leu Glu Pro Val Gln Phe Leu Arg Ser Val Phe Ala Asn Ser Leu Val Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe Arg Lys Asp Met Asp Lys Val Glu Thr Phe Leu Arg Ile Val Gln CysArg Ser Val Glu Gly Ser Cys Gly Phe

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FIG. 71A

ATGGCGCCCGTCGCCGTCTGGGCCGCCGCTCGGACTGGAGCT CTGGGCTGCGGCACGCCTTGCCCGCCCAGGTGGCATTTACACCCTA CGCCCGGAGCCCGGGAGCACATGCCGGCTCAGAGAATACTATGACC AGACAGCTCAGATGTGCTGCAGCAAATGCTCGCCGGGCCAACATGCA AAAGTCTTCTGTACCAAGACCTCGGACACCGTGTGTGACTCCTGTGAG GACAGCACATACACCCAGCTCTGGAACTGGGTTCCCGAGTGCTTGAG CTGTGGCTCCCGCTGTAGCTCTGACCAGGTGGAAACTCAAGCCTGCAC TCGGGAACAGAACCGCATCTGCACCTGCAGGCCCGGCTGGTACTGCG CGCTGAGCAAGCAGGAGGGGTGCCGGCTGTGCGCGCCGCTGCGCAAG TGCCGCCCGGGCTTCGGCGTGGCCAGACCAGGAACTGAAACATCAGA CGTGGTGTGCAAGCCCTGTGCCCCGGGGACGTTCTCCAACACGACTTC ATCCACGGATATTTGCAGGCCCCACCAGATCTGTAACGTGGTGGCCAT CCCTGGGAATGCAAGCATGGATGCAGTCTGCACGTCCACGTCCCCCA ACACGATCCCAACACACGCAGCCAACTCCAGAACCCAGCACTGCTCC AAGCACCTCCTTCCTGCTCCCAATGGGCCCCAGCCCCCAGCTGAAGG GAGCACTGGCGACTTCGCTCTTCCAGTTGGACTGATTGTGGGTGTGAC AGCCTTGGGTCTACTAATAATAGGAGTGGTGAACTGTGTCATCATGAC CCAGGTGAAAAAGAAGCCCTTGTGCCTGCAGAGAGAAGCCAAGGTGC CTCACTTGCCTGCCGATAAGGCCCGGGGTACACAGGGCCCCGAGCAG CAGCACCTGCTGATCACAGCGCCGAGCTCCAGCAGCAGCTCCCTGGA GAGCTCGGCCAGTGCGTTGGACAGAAGGGCGCCCACTCGGAACCAGC CACAGGCACCAGGCGTGGAGGCCAGTGGGGCCGGGAGGCCCGGGC CAGCACCGGGAGCTCAGATTCTTCCCCTGGTGGCCATGGGACCCAGG TCAATGTCACCTGCATCGTGAACGTCTGTAGCAGCTCTGACCACAGCT CACAGTGCTCCTCCCAAGCCAGCTCCACAATGGGAGACACAGATTCC AGCCCCTCGGAGTCCCCGAAGGACGAGCAGGTCCCCTTCTCCAAGGA GGAATGTGCCTTTCGGTCACAGCTGGAGACGCCAGAGACCCTGCTGG GGAGCACCGAAGAGAAGCCCCTGCCCCTTGGAGTGCCTGATGCTGGG ATGAAGCCCAGTTAACCAGGCCGGTGTGGGCTGTGTCGTAGCCAAGG TGGGCTGAGCCCTGGCAGGATGACCCTGCGAAGGGGCCCTGGTCCTT CCAGGC

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FIG. 71B

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His Gin Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys Val lle Met Thr Gin Val Lys Lys Pro Leu Cys Leu Gin Arg Giu Ala Lys Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser

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FIG. 72A

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

FIG. 72B

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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FIG. 73A

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Try Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Try Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser

FIG. 73B

Asp Ile Gin Met Thr Gin Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Cys Gin Leu Ser Val Gly Tyr Met His Trp Tyr Gin Gin Lys Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Giu Phe Thr Leu Thr Ile Ser Ser Leu Gin Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gin Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Gly Thr Lys Leu Glu Ile Lys

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FIG. 74A

GACATCTTGCTGACTCAGTCTCCAGCCATCCTGTCTGTGAGTCCAGGA
GAAAGAGTCAGTTTCTCCTGCAGGGCCAGTCAGTTCGTTGGCTCAAGC
ATCCACTGGTATCAGCAAAGAACAAATGGTTCTCCAAGGCTTCCATA
AAGTATGCTTCTGAGTCTATGTCTGGGATCCCTTCCAGGTTTAGTGGC
AGTGGATCAGGGACAGATTTTACTGTCAACAAGACTCTGGAGTCT
GAAGATATTGCAGATTATTACTGTCAACAAAGTCATAGCTGGCCATTC
ACGTTCGGCTCGGGGACAAATTTGGAAGTAAAAGAAGTGAAGCTTGA
GGAGTCTGGAGGAGGCTTGGTGCAACCTGGAGGATCCATGAAACTTC
CCTGTGTTGCCTCTGGATTCATTTCAGTAACCACTGGATGAAACTTG
TCCGCCAGTCTCCAGAGAAGGGGCTTGAGTGGGTTGCTGAAATTAGA
TCAAAATCTATTAATTCTGCAACACATTATGCGGAGTCTGTGAAAGGG
AGGTTCACCATCTCAAGAGATGATTCCAAAAGTGCTTCTCCAGA
ATGACCGACTTAAGAACTGAAGACACTGGCGTTTATTACTGTCCAGA
AATTACTACGGTAGTACCTACAGG

FIG. 74B

Asp Ile Leu Leu Thr, Gin Ser Pro Ala Ile Leu Ser Val Ser Pro Gly Glu Arg Val Ser Phe Ser Cys Arg Ala Ser Gln Phe Val Gly Ser Ser Ile His Trp Tyr Gln Gln Arg Thr Asn Gly Ser Pro Arg Leu Leu Ile Lys Tyr Ala Ser Glu Ser Met Ser Gly Ile Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Thr Val Glu Ser Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser Cys Val Ala Ser Gly Phe Ile Phe Ser Asn His Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu Ile Arg Ser Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr LeuGin Met Thr Asp Leu Arg Thr Glu Asp Thr Gly Val Tyr Tyr Cys Ser Arg Asn Tyr Tyr Gly Ser Thr Tyr Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val Ser

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FIG. 75A

ATGGAGACAGACACTCCTGTTATGGGTGCTGCTGCTCTGGGTTCCA GGTTCCACTGGTGACGTCAGGCGAGGCCCCGGAGCCTGCGGGGCAG GGACGCCCAGCCCCACGCCCTGCGTCCCGGCCGAGTGCTTCGACC TGCTGGTCCGCCACTGCGTGGCCTGCGGGCTCCTGCGCACGCCGCGC CGAAACCGGCCGGGCCAGCAGCCCTGCGCCCAGGACGCGCTGCAG CCGCAGGAGTCGGTGGGCGCGGGGGGCCGGCGAGGCGGCGGTCGACA AAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGA CCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATC TCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGA AGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGCGTGGAGGTGC ATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTA CCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGG CAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA TCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAG GTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGT CAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGT GGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACG CCTCCCGTGTTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTC ACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC CGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCT CCCTGTCTCCCGGGAAATGA

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FIG. 75B

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Val Arg Arg Gly Pro Arg Ser Leu Arg Gly Arg Asp Ala Pro Ala Pro Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu Leu Val Arg His Cys Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro Lys Pro Ala Gly Ala Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro Gln Glu Ser Val Gly Ala Gly Ala Gly Glu Ala Ala Val Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

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FIG. 76

Asp Ile Gin Met Thr Gin Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gin Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gin Gin Lys Pro Asp Giy Ile Val Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Shr Giy Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gin Giu Asp Ile Ala Thr Tyr Phe Cys Gin Gin Giy Asn Thr Leu Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Giu Ile Lys

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FIG. 77

Gin Vai Gin Leu Gin Gin Ser Giy Ala Giu Leu Vai Giy Pro Giy Thr Ser Val Arg Val Ser Cys Lys Ala Ser Giy Tyr Ala Phe Thr Asn Tyr Leu Ile Giu Trp Val Lys Gin Arg Pro Giy Gin Gly Leu Giu Trp Ile Giy Val Ile Tyr Pro Giy Ser Giy Gly Thr Asn Tyr Asn Giu Lys Phe Lys Giy Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr Met Gin Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys Ala Arg Arg Asp Giy Asn Tyr Giy Trp Phe Ala Tyr Trp Giy Arg Giy Thr Leu Val Thr Val Ser Ala

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FIG. 78

Asp IIe Gin Met Thr Gin Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr IIe Ser Cys Arg Ala Ser Gin Asp IIe Asn Asn Tyr Leu Asn Trp Tyr Gin Gin Lys Pro Giy Lys Ala Pro Lys Leu Leu IIe Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr IIe Ser Ser Leu Gin Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gin Gln Gly Asn Thr Leu Pro Trp Thr Phe Gly Gin Gly Thr Lys Val Glu Val Lys

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FIG. 79

Gin Val Gin Leu Val Gin Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser

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FIG. 80

Asp Ile Gin Met Thr Gin Thr Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gin Asp Ile Asn Asn Tyr Leu Asn Trp Tyr Gin Gin Lys Pro Giy Lys Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gin Pro Asp Asp Phe Ala Thr Tyr Phe Cys Gin Gin Gly Asn Thr Leu Pro Trp Thr Phe Gly Gin Giy Thr Lys Val Giu Val Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gin Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Giu Ala Lys Val Gin Trp Lys Val Asp Asn Ala Leu Gin Ser Gly Asn Ser Gin Giu Ser Val Thr Giu Gin Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Giu Lys His Lys Val Tyr Ala Cys Giu Val Thr His Gin Giy Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Giy Giu Cys

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FIG. 81

Gin Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gin Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gin Gin Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly

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FIG. 82A

ATGGATTTTCAGGTGCAGATTATCAGCTTCCTGCTAATCAGTGCTTCA GTCATAATGTCCAGAGGGCAAATTGTTCTCCCCAGTCTCCAGCAATC CTGTCTGCATCTCCAGGGGAGAAGGTCACAATGACTTGCAGGGCCAG CTCAAGTGTAAGTTACATCACTGGTTCCAGCAGAAGCCAGGATCCTC CCCCAAACCCTGGATTTATGCCACATCCAACCTGGCTTCTGGAGTCCC TGTTCGCTTCAGTGGCAGTGGGTCTGGGACTTCTTACTCTCTCACAAT CAGCAGAGTGGAGGCTGAAGATGCTGCCACTTATTACTGCCAGCAGT GGACTAGTAACCCACCCACGTTCGGAGGGGGGACCAAGCTGGAAATC AAA

FIG. 82B

Met Asp Phe Gin Val Gin Ile Ile Ser Phe Leu Leu Ile Ser Ala Ser Val Ile Met Ser Arg Gly Gln Ile Val Leu Ser Gin Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile His Trp Phe Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

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FIG. 83A

FIG. 83B

Met Gly Trp Ser Leu Ile Leu Leu Phe Leu Val Ala Val Ala Thr Arg Val Leu Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Asn Met His Trp Val Lys Gln Thr Pro Gly Arg Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Gly Asn Gly Asn Thr Ser Tyr Asn Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ala

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CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTG ACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAG AGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGAACACAGACCC GTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGTCGCTGTTGCTA CGCGTGTCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCT CCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTC AAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC CCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA AGGTGGACAAGAAAGCAGAGCCCAAATCTTGTGACAAAACTCACACA TGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTC CTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGT CAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAGA CAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGACTACAA GTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCA TCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG CCCCCATCCCGGGATGAGCTGACCAGGAACCAGGTCAGCCTGACCTG CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG GACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGA GGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGG TAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGTG ACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCCT CCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAA TTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGGTGGGG TGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCA TGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAGC GCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCATA ATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGAT TGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC AATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCAT ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGG

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FIG. 84B

CAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTG ACGCAAATGGGCGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAG AGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGAACACAGACCC GTCGACATGGGTTGGAGCCTCATCTTGCTCTTTCCTTGTCGCTGTTGCTA CGCGTGTCGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCT CCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGTC AAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGC CCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGG CACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA AGGTGGACAAGAAGCAGAGCCCAAATCTTGTGACAAAACTCACACA TGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTC CTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCT GAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGT CAAGTTCAACTGGTACGTGGACGCGTGGAGGTGCATAATGCCAAGA CAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGACTACAA GTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCA TCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTG CCCCATCCCGGGATGAGCTGACCAGGAACCAGGTCAGCCTGACCTG CCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGA GCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG GACTCCGACGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGA GGCTCTGCACACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGG TAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGTG ACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCCT CCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAAA TTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGGG TGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGCA TGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAGC GCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCATA ATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGAT TGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC AATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCAT ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGG

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GCTGCGATTTCGCGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTG GTAGGATTTTATCCCCGCTGCCATCATGGTTCGACCATTGAACTGCAT CGTCGCCGTGTCCCAAAATATGGGGATTGGCAAGAACGGAGACCTAC CCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCCAAAGAATGACC ACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATTATGGGTAG GAAAACCTGGTTCTCCATTCCTGAGAACAATCGACCTTTAAAGGACA GAATTAATATAGTTCTCAGTAGAGAACTCAAAGAACCACCACGAGGA GCTCATTTTCTTGCCAAAAGTTTGGATGATGCCTTAAGACTTATTGAA CAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAGTCGGAGG CAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTTAGACT CTTTGTGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCCC AGAAATTGATTTGGGGAAATATAAACTTCTCCCAGAATACCCAGGCG TCCTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTTGAA GTCTACGAGAAGAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGC TCCCCTCCTAAAGTCATGCATTTTTATAAGACCATGGGACTTTTGCTG TTGCCCCTCCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCAC TGTCCTTTCCTAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAG GTGTCATTCTATTCTGGGGGGTGGGGTGGGGCAGGACAGCAAGGGGG AGGATTGGGAAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCT ATGGAACCAGCTGGGGCTCGAGCTACTAGCTTTGCTTCTAATTTCTT ATTTGCATAATGAGAAAAAAGGAAAATTAATTTTAACACCAATTCA GTAGTTGATTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACA GTGTTCTCTGCACAGATAAGGACAAACATTATTCAGAGGGAGTACCC AGAGCTGAGACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGA AATATGCTTGTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGG TAAGGGCCAATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGG CAGAGCATATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTC TGACATAGTTGTGTTGGGAGCTTGGATCGATCCTCTATGGTTGAACAA GATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTC GGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGT GTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGA CCTGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTAT CGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTG TCACTGAAGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGG CAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATC ATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGC CCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCG GATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATC AGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATG CCCGACGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCG

294/345 FIG. 84D

AATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGC CGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCG TGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGT GCTTTACGGTATCGCCGCTTCCCGATTCGCAGCGCATCGCCTTCTATC GCCTTCTTGACGAGTTCTTCTGAGCGGGACTCTGGGGTTCGAAATGAC CGACCAAGCGACGCCAACCTGCCATCACGAGATTTCGATTCCACCG CCGCCTTCTATGAAAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCG GCTGGATGATCCTCCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCC ACCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATA GCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTT GTGGTTTGTCCAAACTCATCAATCTATCTTATCATGTCTGGATCGCGG CCGCGATCCCGTCGAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCC TGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGG AGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCAC ATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTC GTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTT TGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTC GGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAA TACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGA GCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGC TGGCGTTTTTCCATAGGCTCCGCCCCCTGACGAGCATCACAAAAATC GACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATAC CAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACC CTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTC GTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGAC CGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGA CACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAG AGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTA ACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGA AGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAA CAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATT ACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTCTAC GGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGG TCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAA AATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTG ACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTC TATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTAC GATACGGGAGGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGC GAGACCCACGCTCACCGCCTCCAGATTTATCAGCAATAAACCAGCCA GCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTC

295/345 FIG. 84E

296/345 FIG. 85A

GACGTCGCGGCCGCTCTAGGCCTCCAAAAAAAGCCTCCTCACTACTTCT AAAATTAGTCAGCCATGCATGGGGCGGAGAATGGGCGGAACTGGGCG GAGTTAGGGGCGGATGGGCGGAGTTAGGGGCGGGACTATGGTTGCT GACTAATTGAGATGCATGCTTTGCATACTTCTGCCTGCTGGGGAGCCT ATACTTCTGCCTGCTGGGGAGCCTGGGGACTTTCCACACCCTAACTGA CACACATTCCACAGAATTAATTCCCCTAGTTATTAATAGTAATCAATT ACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAA CTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCC ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGA CTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCACT TGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACG TCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCT TATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA TTACCATGGTGATGCGGTTTTTGGCAGTACATCAATGGGCGTGGATACC GGTTTGACTCACGCGGATTTCCAAGTCTCCACCCCATTGACGTCAATG GGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTA ACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGG GAGGTCTATATAAGCAGAGCTGGGTACGTGAACCGTCAGATCGCCTG GAGACGCCATCACAGATCTCTCACTATGGATTTTCAGGTGCAGATTAT CAGCTTCCTGCTAATCAGTGCTTCAGTCATAATGTCCAGAGGACAAAT TGTTCTCCCAGTCTCCAGCAATCCTGTCTGCATCTCCAGGGGAGAA GGTCACAATGACTTGCAGGGCCAGCTCAAGTGTAAGTTACATCCACT GGTTCCAGCAGAAGCCAGGATCCTCCCCCAAACCCTGGATTTATGCCA CATCCAACCTGGCTTCTGGAGTCCCTGTTCGCTTCAGTGGCAGTGGGT CTGGGACTTCTTACTCTCACAATCAGCAGAGTGGAGGCTGAAGATG GAGGGGGACCAAGCTGGAAATCAAACGTACGGTGGCTGCACCATCT GTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCC TCTGTTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTA CAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAG TGTCACAGAGCAGGACAGCAAGGACACCTACAGCCTCAGCAGCA CCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTT CAACAGGGGAGAGTGTTGAATTCAGATCCGTTAACGGTTACCAACTA CCTAGACTGGATTCGTGACAACATGCGGCCGTGATATCTACGTATGAT CAGCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCCTC CCCCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCC

297/345 FIG. 85B

TAATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCT ATTCTGGGGGTGGGGTGGGGCAGGACAGCAAGGGGGAGGATTGGG AAGACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCA GCTGGGGCTCGACAGCTATGCCAAGTACGCCCCCTATTGACGTCAATG ACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGG ACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCAT GGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTG ACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTT TGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACT CCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTC TATATAAGCAGAGCTGGGTACGTCCTCACATTCAGTGATCAGCACTGA ACACAGACCCGTCGACATGGGTTGGAGCCTCATCTTGCTCTTCCTTGT CGCTGTTGCTACGCGTGTCCTGTCCCAGGTACAACTGCAGCAGCCTGG GGCTGAGCTGGTGAAGCCTGGGGCCTCAGTGAAGATGTCCTGCAAGG CTTCTGGCTACACATTTACCAGTTACAATATGCACTGGGTAAAACAGA CACCTGGTCGGGGCCTGGAATGGATTGGAGCTATTTATCCCGGAAAT GGTGATACTTCCTACAATCAGAAGTTCAAAGGCAAGGCCACATTGAC TGCAGACAAATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGA CATCTGAGGACTCTGCGGTCTATTACTGTGCAAGATCGACTTACTACG GCGGTGACTGGTACTTCAATGTCTGGGGCGCAGGGACCACGGTCACC GTCTCTGCAGCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCC TCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGT CAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCG CCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAG GACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGG GCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACC AAGGTGGACAAGAAAGCAGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCC TGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGG TCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAG ACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAG CGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACA AGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACC ATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCT GCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCT GCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAG AGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCT GGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAA GAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATG AGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG GTAAATGAGGATCCGTTAACGGTTACCAACTACCTAGACTGGATTCGT

298/345 FIG. 85C

GACAACATGCGGCCGTGATATCTACGTATGATCAGCCTCGACTGTGCC ACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTAATAAAATGAGGAA ATTGCATCGCATTGTCTGAGTAGGTGTCATTCTATTCTGGGGGGTGGG GTGGGGCAGGACAGCAAGGGGGAGGATTGGGAAGACAATAGCAGGC ATGCTGGGGATGCGGTGGGCTCTATGGAACCAGCTGGGGCTCGACAG CGCTGGATCTCCCGATCCCCAGCTTTGCTTCTCAATTTCTTATTTGCAT AATGAGAAAAAAAGGAAAATTAATTTTAACACCAATTCAGTAGTTGA TTGAGCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCT GCACAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAG ACTCCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTT GTCATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCC AATCTGCTCACACAGGATAGAGAGGGCAGGAGCCAGGGCAGAGCAT ATAAGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAG TTGTGTTGGGAGCTTGGATAGCTTGGACAGCTCAGGGCTGCGATTTCG CGCCAAACTTGACGGCAATCCTAGCGTGAAGGCTGGTAGGATTTTATC CCCGCTGCCATCATGGTTCGACCATTGAACTGCATCGTCGCCGTGTCC CAAAATATGGGGATTGGCAAGAACGGAGACCTACCCTGGCCTCCGCT CAGGAACGAGTTCAAGTACTTCCAAAGAATGACCACAACCTCTTCAG TGGAAGGTAAACAGAATCTGGTGATTATGGGTAGGAAAACCTGGTTC TCCATTCCTGAGAAGAATCGACCTTTAAAGGACAGAATTAATATAGTT CTCAGTAGAGAACTCAAAGAACCACCACGAGGAGCTCATTTTCTTGC CAAAAGTTTGGATGATGCCTTAAGACTTATTGAACAACCGGAATTGG CAAGTAAAGTAGACATGGTTTGGATAGTCGGAGGCAGTTCTGTTTACC AGGAAGCCATGAATCAACCAGGCCACCTTAGACTCTTTGTGACAAGG ATCATGCAGGAATTTGAAAGTGACACGTTTTTCCCAGAAATTGATTTG GGGAAATATAAACTTCTCCCAGAATACCCAGGCGTCCTCTCTGA GGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTTGAAGTCTACGAGA AGAAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGCTCCCCTCCTAA AGCTATGCATTTTATAAGACCATGGGACTTTTGCTGGCTTTAGATCA GCCTCGACTGTGCCTTCTAGTTGCCAGCCATCTGTTGTTTGCCCCCTCCC CCGTGCCTTCCTTGACCCTGGAAGGTGCCACTCCCACTGTCCTTTCCTA ATAAAATGAGGAAATTGCATCGCATTGTCTGAGTAGGTGTCATTCTAT TCTGGGGGGTGGGGTGGGCAGGACAGCAAGGGGGAGGATTGGGAA GACAATAGCAGGCATGCTGGGGATGCGGTGGGCTCTATGGAACCAGC TGGGGCTCGAGCTACTAGCTTTGCTTCTCAATTTCTTATTTGCATAATG GCAAATGCGTTGCCAAAAAGGATGCTTTAGAGACAGTGTTCTCTGCA CAGATAAGGACAAACATTATTCAGAGGGAGTACCCAGAGCTGAGACT CCTAAGCCAGTGAGTGGCACAGCATTCTAGGGAGAAATATGCTTGTC ATCACCGAAGCCTGATTCCGTAGAGCCACACCTTGGTAAGGGCCAAT CTGCTCACACAGGATAGAGAGGGCAGGGCAGGGCAGAGCATATA AGGTGAGGTAGGATCAGTTGCTCCTCACATTTGCTTCTGACATAGTTG

299/345 FIG. 85D

TGTTGGGAGCTTGGATCGATCCTCTATGGTTGAACAAGATGGATTGCA CGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTG GGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTC AGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGC CGACGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGG GAAGGGACTGCCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTG TCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCA ATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCAC CAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGG TCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGC CAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAG GATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTG GAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTG GCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGA AGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTAT CGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGA GCCCAACCTGCCATCACGAGATTTCGATTCCACCGCCGCCTTCTATGA AAGGTTGGGCTTCGGAATCGTTTTCCGGGACGCCGGCTGGATGATCCT CCAGCGCGGGGATCTCATGCTGGAGTTCTTCGCCCACCCCAACTTGTT TATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTT CACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGGTTTGTCCAA ACTCATCAATCTATCTTATCATGTCTGGATCGCGGCCGCGATCCCGTC GAGAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGT TATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTG TAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTT GCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCA TTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGC GCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCT GCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCA CAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCA GCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCC ATAGGCTCCGCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGT CAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC CCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTAC CGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCA ATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAA GCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTT ATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATC

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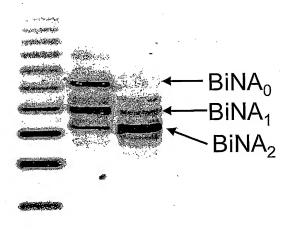
FIG. 53A

GCGCCTCTTATGTACCCACAAAAATCTATTTTCAAAAAAGTTGCTCTA AGAATATAGTTATCAAGTTAAGTAAAATGTCAATAGCCTTTTAATTTA ATTTTTAATTGTTTTATCATTCTTTGCAATAATAAAACATTAACTTTAT ACTTTTTAATTTAATGTATAGAATAGAGATATACATAGGATATGTAAA TAGATACACAGTGTATATGTGATTAAAATATAATGGGAGATTCAATC AATAATGAAAAAAATGTGGTGAGAAAAACAGCTGAAAACCCATGTA AAGAGTGTATAAAGAAAGCAAAAAGAGAAGTAGAAAGTAACACAGG GGCATTTGGAAAATGTAAACGAGTATGTTCCCTATTTAAGGCTAGGC ACAAAGCAAGGTCTTCAGAGAACCTGGAGCCTAAGGTTTAGGCTCAC CCATTTCAACCAGTCTAGCAGCATCTGCAACATCTACAATGGCCTTGA CCTTTGCTTTACTGGTGGCCCTCCTGGTGCTCAGCTGCAAGTCAAGCT GCTCTGTGGGCTGTGATCTGCCTCAAACCCACAGCCTGGGTAGCAGG AGGACCTTGATGCTCCTGGCACAGATGAGGAGAATCTCTCTTTTCTCC TGCTTGAAGGACAGACATGACTTTGGATTTCCCCAGGAGGAGTTTGG CAACCAGTTCCAAAAGGCTGAAACCATCCCTGTCCTCCATGAGATGA TCCAGCAGATCTTCAATCTCTTCAGCACAAAGGACTCATCTGCTGCTT GGGATGAGACCCTCCTAGACAAATTCTACACTGAACTCTACCAGCAG CTGAATGACCTGGAAGCCTGTGTGATACAGGGGGTGGGGGTGACAGA GACTCCCCTGATGAAGGAGGACTCCATTCTGGCTGTGAGGAAATACT TCCAAAGAATCACTCTCTATCTGAAAGAGAAGAAATACAGCCCTTGT GCCTGGGAGGTTGTCAGAGCAGAAATCATGAGATCTTTTTCTTTGTCA ACAAACTTGCAAGAAAGTTTAAGAAGTAAGGAATGAAAACTGGTTCA ACATGGAAATGATTTCATTGATTCGTATGCCAGCTCACCTTTTTATG ATCTGCCATTTCAAAGACTCATGTTTCTGCTATGACCATGACACGATT TAAATCTTTTCAAATGTTTTTAGGAGTATTAATCAACATTGTATTCAG ATCTATTTAAATATTTTTAAAATATTATTTATTTAACTATTTATAAAAAC AACTTATTTTTGTTCATATTATGTCATGTGCACCTTTGCACAGTGGTTA CATTGAACTTTTGCTATGGAACTTTTGTACTTGTTTATTCTTTAAAATG AAATTCCAAGCCTAATTGTGCAACCTGATTACAGAATAACTGGTACA CTTCATTTGTCCATCAATATTATATTCAAGATATAAGTAAAAATAAAC TTTCTGTAAACCAAGTTGTATGTTGTACTCAAGATAACAGGGTGAACC TAACAAATACAATTCTGCTCTCTTGTGTATTTGATTTTTGTATGAAAA AAACTAAAAATGGTAATCATACTTAATTATCAGTTATGGTAAATGGT ATGAAGAGAAGAAGGAACG

300/345 FIG. 85E

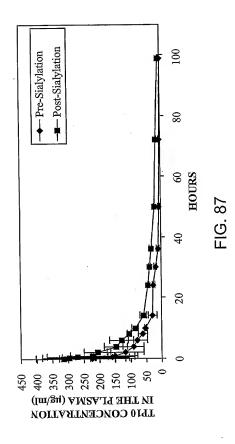
GCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATG TAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTAC ACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACC TGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAA AAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGC TCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATC AAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAA ATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATG CTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCC ATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGG CTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTC ACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCG ATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGC GCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGT TTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGCGAGTTA CATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTC CGATCGTTGTCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTA TGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGCT TTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTA TGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACC GCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCT TCGGGGCGAAAACTCTCAAGGATCTTACCGCTGTTGAGATCCAGTTCG ATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTCA CCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAA AAGGGAATAAGGGCGACACGGAAATGTTGAATACTCATACTCTTCCT TTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGG ATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTCCGC GCACATTTCCCCGAAAAGTGCCACCT

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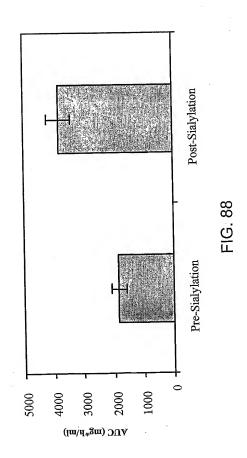


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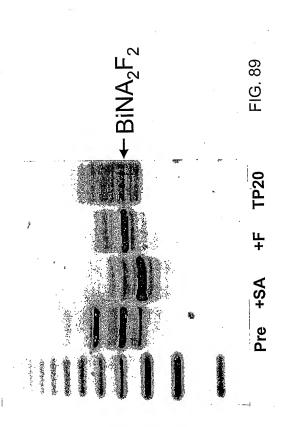
FIG. 86

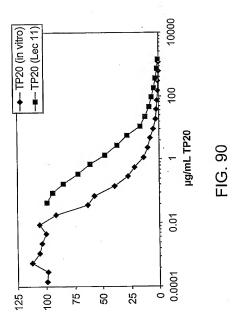


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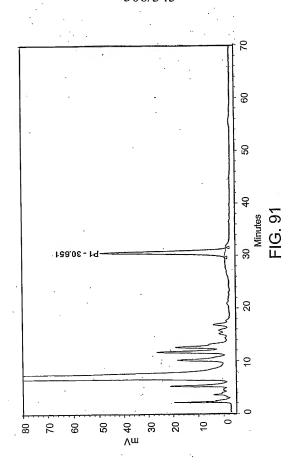


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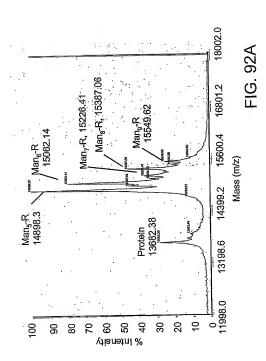


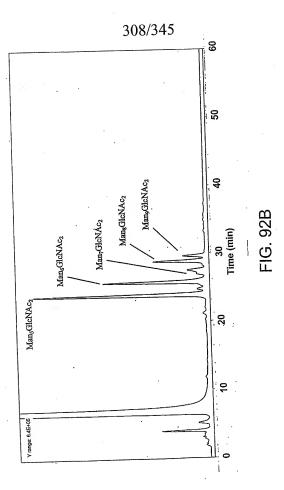


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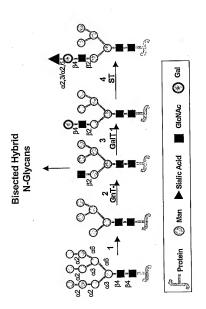
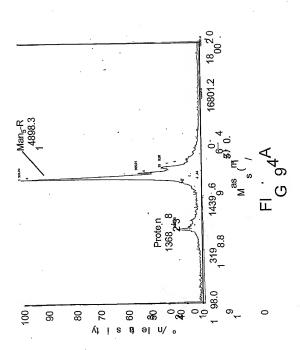
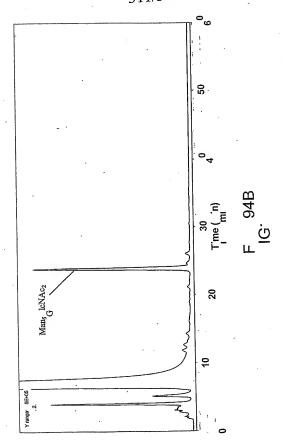


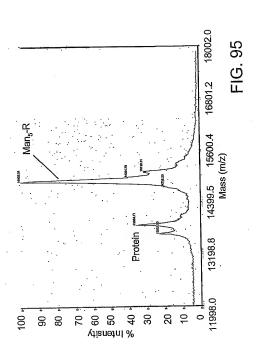
FIG. 93

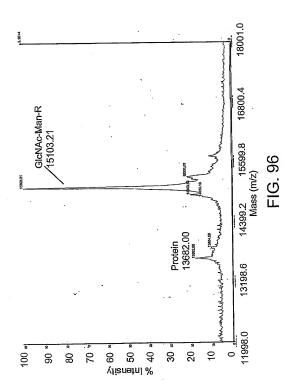


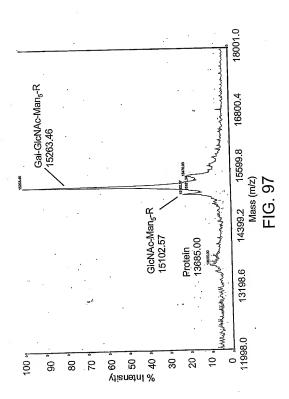
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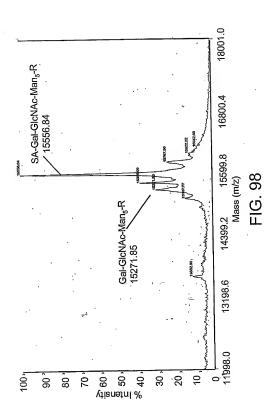


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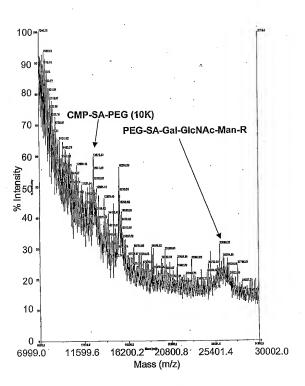


FIG. 99A

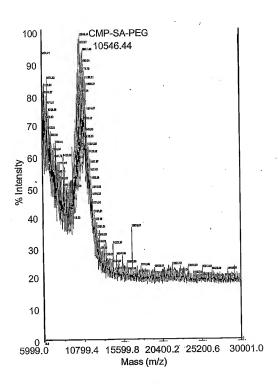
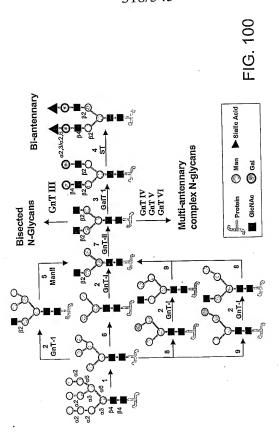
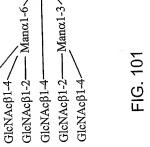


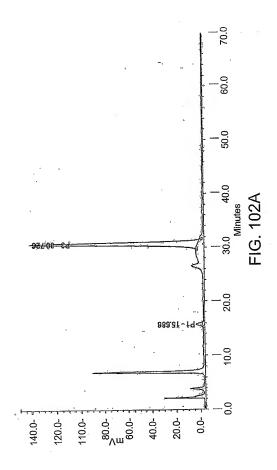
FIG. 99B

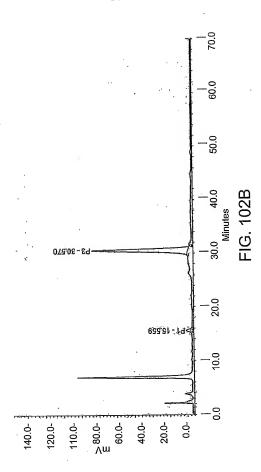


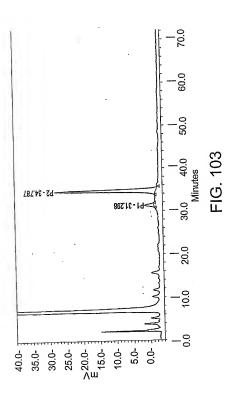


GlcNAcβ1-6

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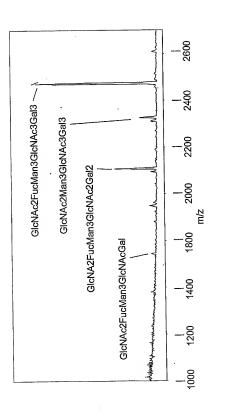


FIG. 104

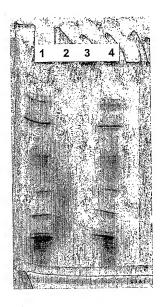


FIG. 105

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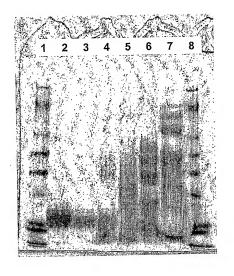


FIG. 106

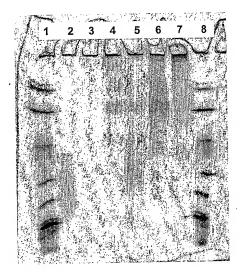


FIG. 107

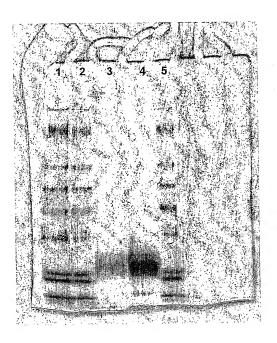


FIG. 108

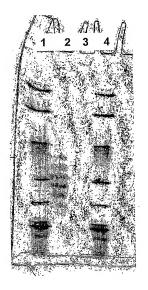


FIG. 109

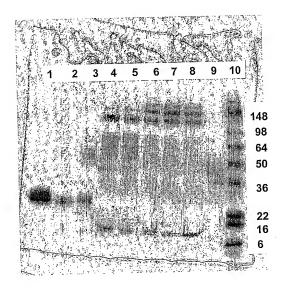


FIG. 110

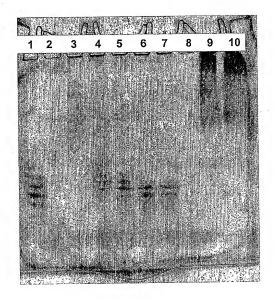
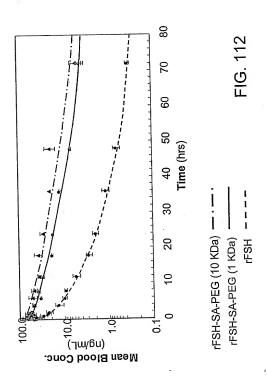
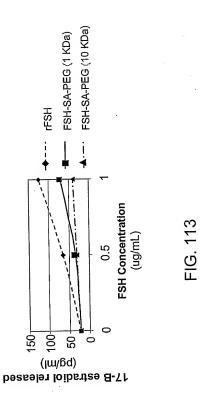


FIG. 111





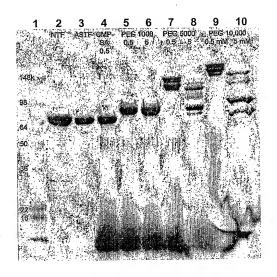


FIG. 114

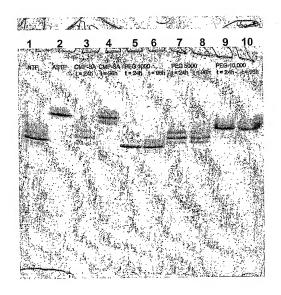


FIG. 115

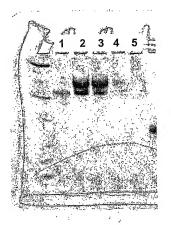
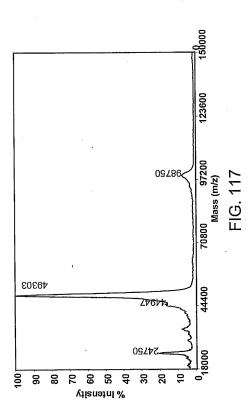
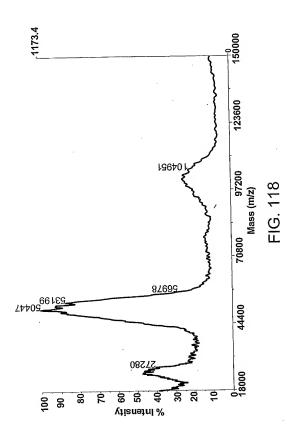
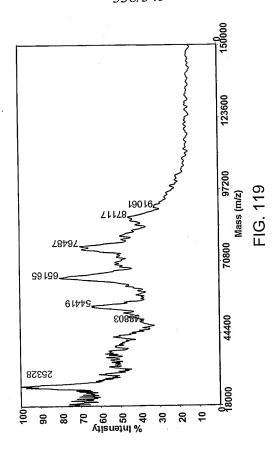


FIG. 116

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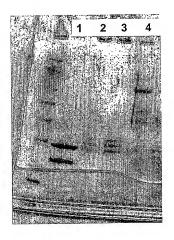


FIG. 120

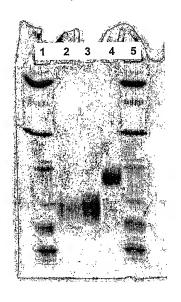


FIG. 121

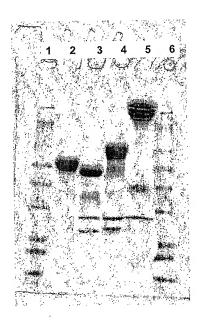
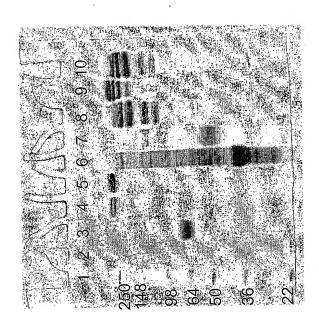


FIG. 122



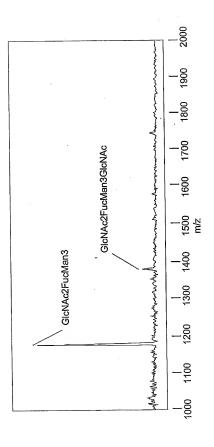


FIG. 124

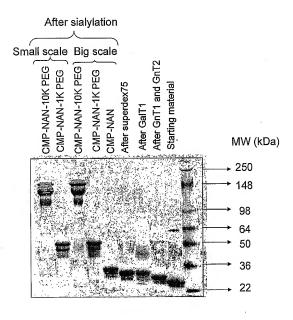


FIG. 125

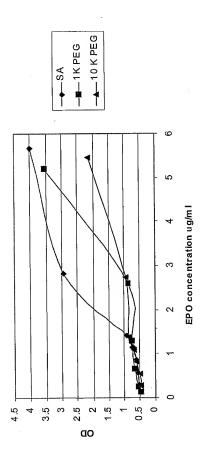


FIG. 126

SEQUENCE LISTING

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Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys
50 60

Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser 65 70 75 80

Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser 85 90 95

Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp 100 105

Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro 115 120 125

Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe 130 135 140

Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe

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160 155 145 150

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Leu Phe Ser Cys 50	Leu Lys Asp 55	Arg His	Asp Phe	Gly Phe E 60	ro Gln	Glu	
Glu Phe Gly Asn 65	Gln Phe Gln 70	Lys Ala	Glu Thr 75	Ile Pro V	/al Leu	His 80	
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Ala Ala Trp Asp	Glu Thr Leu	Leu Asp 105	Lys Phe	Tyr Thr	3lu Leu 110	Tyr	
Gln Gln Leu Asn 115	. Asp Leu Glu	Ala Cys 120	val Ile	Gln Gly 1 125	Val Gly	Val	
Thr Glu Thr Pro	Leu Met Lys	Glu Asp	Ser Ile	Leu Ala	Val Arg	Lys	

140

135

130

Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro 145 1.50 Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu 180 <210> 5 <211> 757 <212> DNA <213> Homo sapiens <400> 5 atgaccaaca agtgtctcct ccaaattgct ctcctgttgt gcttctccac tacagctctt 60 tccatgagct acaacttgct tggattccta caaagaagca gcaattttca gtgtcagaag 120 ctcctgtggc aattgaatgg gaggcttgaa tattgcctca aggacaggat gaactttgac 180 atccctgagg agattaagca gctgcagcag ttccagaagg aggacgccgc attgaccatc 240 tatgagatgc tccagaacat ctttgctatt ttcagacaag attcatctag cactggctgg 300 aatgagacta ttgttqagaa cctcctggct aatgtctatc atcagataaa ccatctgaag 360 acagtcctgg aagaaaaact ggagaaagaa gattttacca ggggaaaact catgagcagt 420 ctgcacctga aaagatatta tgggaggatt ctgcattacc tgaaggccaa ggagtacagt 480 cactgtgcct ggaccatagt cagagtggaa atcctaagga acttttactt cattaacaga 540 cttacaggtt acctccgaaa ctgaagatct cctagcctgt ccctctggga ctggacaatt 600 getteaagea ttetteaace ageagatget gtttaagtga etgatggeta atgtactgea 660 aatgaaagga cactagaaga ttttgaaatt tttattaaat tatgagttat ttttattat 720 757 ttaaatttta ttttggaaaa taaattattt ttggtgc <210> 6 <211> 187 <212> PRT <213> Homo sapiens <400> 6 Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser

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Leu	Glu 50	Tyr	Cys	Leu	Lys	Asp 55	Arg	Met	Asn	Phe	Asp 60	Ile	Pro	Glu	Glu	
Ile 65	ГÀЗ	Gln	Leu	Gln	Gln 70	Phe	Gln	Ьув	Glu	Авр 75	Ala	Ala	Leu	Thr	Ile 80	
Tyr	Glu	Met	Leu	Gln 85	Asn	Ile	Phe	Ala	Ile 90	Phe	Arg	Gln	Asp	Ser 95	Ser	
Ser	Thr	Gly	Trp 100	Asn	Glu	Thr	Ile	Val 105	Glu	Asn	Leu	Leu	Ala 110	Asn	Val	
Tyr	His	Gln 115		Asn	His	Leu	Lys 120	Thr	Val	Leu	Glu	Glu 125	ьув	Leu	Glu	
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His	Cys	Ala	Trp	Thr 165	Ile	val	. Arg	y Val	. Glu 170	ı Il∈	e Let	ı Arg) Ası	175	Tyr	
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240

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Leu His Arg Arg Arg Arg Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro \$35\$

Gly Ser Leu Glu Arg Glu Cys Lys Glu Glu Glu Cys Ser Phe Glu Glu 50 50 60

- Ala Arg Glu Ile Phe Lys Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile 65 70 75 80
- Ser Tyr Ser Asp Gly Asp Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly 85 90 95
- Gly Ser Cys Lys Asp Gln Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro 100 105 110
- Ala Phe Glu Gly Arg Asn Cys Glu Thr His Lys Asp Asp Gln Leu Ile 115 120 125
- Cys Val Asn Glu Asn Gly Gly Cys Glu Gln Tyr Cys Ser Asp His Thr 130 135 140
- Gly Thr Lys Arg Ser Cys Arg Cys His Glu Gly Tyr Ser Leu Leu Ala 145 150 150 155
- Asp Gly Val Ser Cys Thr Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile 165 170 175
- Pro Ile Leu Glu Lys Arg Asn Ala Ser Lys Pro Gln Gly Arg Ile Val. 180 185 190
- Gly Gly Lys Val Cys Pro Lys Gly Gly Cys Pro Trp Gln Val Leu Leu 195 200 205
- Leu Val Asn Gly Ala Gln Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile 210 220
- Trp Val Val Ser Ala Ala His Cys Phe Asp Lys Ile Lys Asn Trp Arg 225 230 235
- Asn Leu Ile Ala Val Leu Gly Glu His Asp Leu Ser Glu His Asp Gly $245 \hspace{1cm} 250 \hspace{1cm} 255$
- Asp Glu Gln Ser Arg Arg Val Ala Gln Val Ile Ile Pro Ser Thr Tyr 260 265 270

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Pro	Val 290	Val	Leu	Thr	Asp	His 295	V al	Val	Pro	Leu	300 300	Leu	Pro	Glu	Arg	
Thr 305	Phe	ser	Glu	Arg	Thr 310	Leu	Ala	Phe	V al	Arg 315	Phe	Ser	Leu	Val	Ser 320	
Gly	Trp	Gly	Gln	Leu 325	Leu	Asp	Arg	Gly	Ala 330	Thr	Ala	Leu	Glu	Leu 335	Met	
Val	Leu	Asn	Val 340	Pro	Arg	Leu	Met	Thr 345	Gln	Asp	Cys	Leu	Gln 350	Gln	Ser	
Arg	Гув	Val 355	Gly	Asp	Ser	Pro	Asn 360	Ile	Thr	Glu	Тут	Met 365	Phe	Сув	Ala	
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Pro 385		Ala	Thr	His	Туг 390	Arg	Gly	Thr	Trp	Tyr 395	Let	Thr	Gly	' Ile	Val 400	
Ser	Trp	Gly	Gln	Gly 405	Сув	Ala	Thr	Val	. Gly 410	His	Phe	e Gly	v Val	. Tyr 415	Thr	
Arg	Val	Ser	Glr 420		: Ile	Glu	Trp	425	Glr	ı Lys	Le	ı Met	430	g Ser	Glu	
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60 120

180

PCT/US02/32263 WO 03/031464

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- Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile \$245\$

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Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60 \hspace{1.5cm}$

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Tyr	Asp	Leu	гЛа	Ser 325	Val	Leu	G1A	Gln	Leu 330	G1y	Ile	Thr	Lys	Val 335	Phe
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Pro 385	Pro	Glu	Val	Lys	Phe 390	Asn	Lys	Pro	Phe	Val 395	Phe	Leu	Met	Ile	Glu 400
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Ser Thr Arg Ser Gly Arg Arg Met Glu Leu Ser Met Gly Pro Ile Gln 85 90 95

Ala Asn His Thr Gly Thr Gly Leu Leu Leu Thr Leu Gln Pro Glu Gln 100 105 110

Lys Phe Gln Lys Val Lys Gly Phe Gly Gly Ala Met Thr Asp Ala Ala 115 120 125

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- Asn Glu Pro Ser Ala Gly Leu Leu Ser Gly Tyr Pro Phe Gln Cys Leu 275 280 285
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- Leu Asp Phe Leu Ala Pro Ala Lys Ala Thr Leu Gly Glu Thr His Arg 355 360 365
- Leu Phe Pro Asn Thr Met Leu Phe Ala Ser Glu Ala Cys Val Gly Ser 370 375 380
- Lys Phe Trp Glu Gln Ser Val Arg Leu Gly Ser Trp Asp Arg Gly Met 385 390 395
- Gln Tyr Ser His Ser Ile Ile Thr Asn Leu Leu Tyr His Val Val Gly 405 410 415
- Trp Thr Asp Trp Asn Leu Ala Leu Asn Pro Glu Gly Gly Pro Asn Trp 420 425 430
- Val Arg Asn Phe Val Asp Ser Pro Ile Ile Val Asp Ile Thr Lys Asp 435 440 445

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Phe Ile Pro Glu Gly Ser Gln Arg Val Gly Leu Val Ala Ser Gln Lys 465 470 475 480

Asn Asp Leu Asp Ala Val Ala Leu Met His Pro Asp Gly Ser Ala Val 485 490 495

Val Val Leu Asn Arg Ser Ser Lys Asp Val Pro Leu Thr Ile Lys 500 505 510

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Ile Tyr Gln Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn 50 60

Arg Val Glu Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser 65 70 75 80

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- Asn Tyr Cys Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val
- Phe Lys Ala Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys 195 200
- Ser Glu Gly Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg 210 215 220
- Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn 225 230 235 240
- Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly 260 265
- Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp 275 280 285
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290 295 300

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Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val 515 520 525

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Asn	Gly 50	Ile	Asn	Asn	Tyr	Lys 55	Asn	Pro	Гуs	Leu	Thr 60	Arg	Met	Leu	Thr	
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Сув	Leu	Glu	Glu	Glu 85	Leu	Lys	Pro	Leu	Glu 90	Glu	Val	Leu	Asn	Leu 95	Ala	
Gln	Ser	Ьув	Asn 100	Phe	His	Leu	Arg	Pro 105	Arg	Asp	Leu	Ile	Ser 110	Asn	Ile '	
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ccaaaactag	cattcttaaa	ctgagaatta	tagatggggt	tcaagaatcc	ctaagtcccc	7740
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<210> 30 <211> 2351

<212> PRT <213> Homo sapiens

<400> 30

Met Gln Ile Glu Leu Sex Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe 1 10 15

Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser 20 25 30

Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg

Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val 50 55 60

Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile 65 70 75 80

Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln 85 90 95

Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser 100 105 110

- His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser 115 120 125
- Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp 130 135 140
- Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu 145 150 150 155 160
- Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser 165 170 175
- Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile 180 185
- Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr 195 200 205
- Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly 210 215
- Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp 225 230 230 235
- Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr \$245\$ \$250\$
- Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
- Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
- Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser 290 295 300
- Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met 305 310 315 320

Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His 325 330 335

- Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro $340 \hspace{1cm} 345 \hspace{1cm} 345 \hspace{1cm} 350 \hspace{1cm}$
- Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp 355 360 365
- Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
- Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr 385 390 395 400
- Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
 405 410 410
- Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn 420 425 430
- Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met 435 440 445
- Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu 450 455 460
- Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu 465 470 475 480
- Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro 485 495
- His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys 500 505
- Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe 515 520 525
- Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp 530 535
- Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg

545 550 555 560

Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu 565 570 575

Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val

Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu 595 600 605

Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp 610 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val 625 630 635 640

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp 645 650 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe 660 665 670

Ser Gly Tyr Thr Phé Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr 675 680 685

Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro 690 695 700

Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly 705 710 715 720

Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp 725 730 735

Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys 740 745

Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Arg 755 760 765

Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Asp 770 775 780

Ile Glu Lys Thr Asp Pro Trp Phe Ala His Arg Thr Pro Met Pro Lys Ile Gln Asn Val Ser Ser Ser Asp Leu Leu Met Leu Leu Arg Gln Ser Pro Thr Pro His Gly Leu Ser Leu Ser Asp Leu Gln Glu Ala Lys Tyr Glu Thr Phe Ser Asp Asp Pro Ser Pro Gly Ala Ile Asp Ser Asn Asn Ser Leu Ser Glu Met Thr His Phe Arg Pro Gln Leu His His Ser Gly Asp Met Val Phe Thr Pro Glu Ser Gly Leu Gln Leu Arg Leu Asn Glu Lys Leu Gly Thr Thr Ala Ala Thr Glu Leu Lys Lys Leu Asp Phe Lys Val Ser Ser Thr Ser Asn Asn Leu Ile Ser Thr Ile Pro Ser Asp Asn Leu Ala Ala Gly Thr Asp Asn Thr Ser Ser Leu Gly Pro Pro Ser Met Pro Val His Tyr Asp Ser Gln Leu Asp Thr Thr Leu Phe Gly Lys Lys Ser Ser Pro Leu Thr Glu Ser Gly Gly Pro Leu Ser Leu Ser Glu Glu Asn Asn Asp Ser Lys Leu Leu Glu Ser Gly Leu Met Asn Ser Gln Glu Ser Ser Trp Gly Lys Asn Val Ser Ser Thr Glu Ser Gly Arg Leu Phe Lys Gly Lys Arg Ala His Gly Pro Ala Leu Leu Thr Lys Asp Asn Ala

Leu Phe Lys Val Ser Ile Ser Leu Leu Lys Thr Asn Lys Thr Ser Asn Asn Ser Ala Thr Asn Arg Lys Thr His Ile Asp Gly Pro Ser Leu Leu Ile Glu Asn Ser Pro Ser Val Trp Gln Asn Ile Leu Glu Ser Asp Thr Glu Phe Lys Lys Val Thr Pro Leu Ile His Asp Arg Met Leu Met Asp Lys Asn Ala Thr Ala Leu Arg Leu Asn His Met Ser Asn Lys Thr Thr Ser Ser Lys Asn Met Glu Met Val Gln Gln Lys Lys Glu Gly Pro Ile Pro Pro Asp Ala Gln Asn Pro Asp Met Ser Phe Phe Lys Met Leu Phe Leu Pro Glu Ser Ala Arg Trp Ile Gln Arg Thr His Gly Lys Asn Ser Leu Asn Ser Gly Gln Gly Pro Ser Pro Lys Gln Leu Val Ser Leu Gly Pro Glu Lys Ser Val Glu Gly Gln Asn Phe Leu Ser Glu Lys Asn Lys Val Val Val Gly Lys Gly Glu Phe Thr Lys Asp Val Gly Leu Lys Glu Met Val Phe Pro Ser Ser Arg Asn Leu Phe Leu Thr Asn Leu Asp Asn Leu His Glu

Asn Asn Thr His Asn Gln Glu Lys Lys Ile Gln Glu Glu Ile Glu 1205 1210 1215

Lys Lys Glu Thr Leu Ile Gln Glu Asn Val Val Leu Pro Gln Ile 1220 1225 1230

- His Thr Val Thr Gly Thr Lys Asn Phe Met Lys Asn Leu Phe Leu 1235 1240 1245
- Leu Ser Thr Arg Gln Asn Val Glu Gly Ser Tyr Asp Gly Ala Tyr 1250 1255 1260
- Ala Pro Val Leu Gln Asp Phe Arg Ser Leu Asn Asp Ser Thr Asn 1265 1270 1270
- Arg Thr Lys Lys His Thr Ala His Phe Ser Lys Lys Gly Glu Glu 1280 1285 1290
- Glu Asn Leu Glu Gly Leu Gly Asn Gln Thr Lys Gln Ile Val Glu 1295 1300 1305
- Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln 1310 1315 1320
- Asn Phe Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg 1325 1330 1335
- Leu Pro Leu Glu Glu Thr Glu Leu Glu Lys Arg Ile Ile Val Asp 1340 1345 1350
- Asp Thr Ser Thr Gln Trp Ser Lys Asn Met Lys His Leu Thr Pro 1355 1360 1360
- Ser Thr Leu Thr Gln Ile Asp Tyr Asn Glu Lys Glu Lys Gly Ala 1370 1375 1380
- Ile Thr Gln Ser Pro Leu Ser Asp Cys Leu Thr Arg Ser His Ser 1385
- Ile Pro Gln Ala Asn Arg Ser Pro Leu Pro Ile Ala Lys Val Ser 1400 1400
- Ser Phe Pro Ser Ile Arg Pro Ile Tyr Leu Thr Arg Val Leu Phe 1415 1420 1425
- Gln Asp Asn Ser Ser His Leu Pro Ala Ala Ser Tyr Arg Lys Lys

1430 1435 1440

Asp Ser Gly Val Gln Glu Ser Ser His Phe Leu Gln Gly Ala Lys

- Lys Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr Gly 1460 1460 1460
- Asp Gln Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser 1475 1485
- Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp 1490 1495 1500
- Leu Pro Lys Thr Ser Gly Lys Val Glu Leu Leu Pro Lys Val His 1505 1510 1515
- Ile Tyr Gln Lys Asp Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser 1520 1525 1530
- Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu Leu Gln Gly Thr 1535 1540 1545
- Glu Gly Ala Ile Lys Trp Asn Glu Ala Asn Arg Pro Gly Lys Val 1550 1560
- Pro Phe Leu Arg Val Ala Thr Glu Ser Ser Ala Lys Thr Pro Ser 1565 1570 1575
- Lys Leu Leu Asp Pro Leu Ala Trp Asp Asn His Tyr Gly Thr Gln 1580 1585 1590
- Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu Lys Ser Pro Glu Lys 1595 1600 1605
- Thr Ala Phe Lys Lys Lys Asp Thr Ile Leu Ser Leu Asn Ala Cys 1610 1615 1620
- Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly Gln Asn Lys 1625 1630 1635

Leu Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile . 1690 Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser . 1740 Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu 1.835 Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu

Lvs Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly

Ile Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly

Met Ser Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro

Leu Gly Met Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala

Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His

Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser

- Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile 2090 2095 2100
- Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser
- Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln Thr 2120 2125 2130
- Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn 2135 2140 2145
- Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile 2150 2155 2160
- Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg 2165 2170 · 2175
- Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys 2180 2185 2190
- Ser Met | Pro Leu Gly Met Glu | Ser Lys Ala Ile | Ser | Asp Ala Gln | 2195 | 2200 |
- Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser 2210 2215
- Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp 2225 2230 2235
- Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe 2240 2245
- Gln Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys 2255 2265
- Ser Leu Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser 2270 2275 2280
- Ser Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys

2285 2290 2295

Val Lys Val Phe Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val 2300 2305

Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr Leu Arg Ile His 2315 2320 2325

Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met Glu Val Leu 2330 2340

Gly Cys Glu Ala Gln Asp Leu Tyr 2345 2350

<210> 31 <211> 1471

<212> DNA

<213> Homo sapiens

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PCT/US02/32263 WO 03/031464

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agggegeeca	ctcggaacca	gccacaggca	ccaggcgtgg	aggccagtgg	ggccggggag	1080
gcccgggcca	gcaccgggag	ctcagattct	tcccctggtg	gccatgggac	ccaggtcaat	1140
gtcacctgca	tcgtgaacgt	ctgtagcagc	tctgaccaca	gctcacagtg	ctcctcccaa	1200
gccagctcca	caatgggaga	cacagattcc	agcccctcgg	agtccccgaa	ggacgagcag	1260
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ctggggagca	ccgaagagaa	gaccatgaca	cttggagtgc	ctgatgctgg	gatgaagccc	1380
	geeggtgtgg					1440
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<210> 32 <211> 461

<212> PRT

<213> Homo sapiens

<400> 32

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu

Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr 25

Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln 40

Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys 55 50

Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp 70 75 65

Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys 85

Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg 105 100

Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu 120 115

Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg 130 Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val 150 145 Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr 170 165 Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly 180 185 Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser 200 195 Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser 215 220 210 Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser 240 230 235 225

Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly 245 250 255

Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly 260 265 270

Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro 290 295 300

Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu 305 . 310 315 320

Ile Thr Ala Pro Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser 325 330 335

Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly 340 345 350

Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser 355 Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile 375 Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln 395 385 390 Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro 405 410 Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser 425 420 Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro 445 435 440 Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser 455 <210> 33 <211> 1475 <212> DNA <213> Homo sapiens <400> 33 tecacetgte ecegeagege eggetegege ceteetgeeg cagecacega geogecqtet 60 agogococga cotogocaco atgagagoco tgotggogog cotgettoto tgogtoctgg 120 tcgtgagcga ctccaaaggc agcaatgaac ttcatcaagt tccatcgaac tgtgactgtc 180 taaatggagg aacatgtgtg tccaacaagt acttetecaa catteaetgg tgcaaetgee 240

caaagaaatt cggagggcag cactgtgaaa tagataagtc aaaaacctgc tatgagggga 300 atggtcactt ttaccgagga aaggccagca ctgacaccat gggccggccc tgcctgccct 360 ggaactetge cactgteett cagcaaacgt accatgeeca cagatetgat getetteage 420 tqqqcctgqg gaaacataat tactgcagga acccagacaa ccggaggcga ccctggtgct 480 atgtgcaggt gggcctaaag ccgcttgtcc aagagtgcat ggtgcatgac tgcgcagatg 540 qaaaaaaqcc ctcctctcct ccagaagaat taaaatttca gtgtggccaa aagactctga 600 ggccccgctt taagattatt gggggagaat tcaccaccat cgagaaccag ccctggtttg 660 eggecateta caggaggeac eggggggget etgteaceta egtgtgtgga ggeagcetea 720

tcagcccttg c	tgggtgatc	agcgccacac	actgcttcat	tgattaccca	aagaaggagg	780
actacatogt c	tacctgggt	cgctcaaggc	ttaactccaa	cacgcaaggg	gagatgaagt	840
ttgaggtgga a	aacctcatc	ctacacaagg	actacagcgc	tgacacgctt	geteaceaca	900
acgacattgc c	ttgctgaag	atccgttcca	aggagggcag	gtgtgcgcag	ccatcccgga	960
ctatacagac c	atctgcctg	ccctcgatgt	ataacgatcc	ccagtttggc	acaagctgtg	1020
agatcactgg c	tttggaaaa	gagaatteta	ccgactatct	ctatccggag	cagctgaaga	1080
tgactgttgt g	aagctgatt	tcccaccggg	agtgtcagca	gccccactac	tacggctctg	1140
aagtcaccac c	aaaatgctg	tgtgctgctg	acccacagtg	gaaaacagat	tcctgccagg	1200
gagactcagg g	ggacccctc	gtctgttccc	tccaaggccg	catgactttg	actggaattg	1260
tgagctgggg c	cgtggatgt	gccctgaagg	acaagccagg	cgtctacacg	agagtctcac	1320
acttcttacc c	tggatccgc	agtcacacca	aggaagagaa	tggcctggcc	ctctgagggt	1380
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catctccatc a				•		1475

<210> 34 <211> 431

<211> 431 <212> PRT

<213> Homo sapiens

<400> 34

Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser 1 10 15

Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp 20 25 30

Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile

His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile 50 60

Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly 65 70 75 80

Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser

Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu 100 105 110

- Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg 115 120 125
 - Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
 - Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro 145 150 160
 - Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg 165 170 175
 - Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp 180 185 190
 - Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val 195 $200 \cdot 205$
 - Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His 210 220
 - Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly 225 \$230\$
 - Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val 245 250 250
 - Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His
 - His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys 275 280 285
 - Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr 290 295 300
 - Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys 305 310 315

Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val 325 325 330 335

Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly

Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys 355 360

Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu 370 375 380

Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys 385 390 395 400

Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu 405 415

Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
420 425 430

<210> 35

<211> 107

<212> PRT

<213> Mus musculus

<400> 35

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala $_{20}^{}$

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile 35 40 . 45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly 50 $$ 55 $$ 60

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro

85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

<210> 36

<211> 120 <212> PRT

<213> Mus musculus

<400> 36

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr 20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln 100 105 110

Gly Thr Leu Val Thr Val Ser Ser 115 120

<210> 37 <211> 120

<211> 120

<213> Mus musculus

<400> 37

Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln 1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser 20 25 30

Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Ala Leu Glu 35 40 45

Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp Tyr Asn Pro Ser 50 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val 65 70 75 80

Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr 85 90 95

Cys Ala Arg Ser Met Ile Thr Asn Trp Tyr Phe Asp Val Trp Gly Ala $100 \\ 105$

Gly Thr Thr Val Thr Val Ser Ser 115 120

<210> 38

<211> 106 <212> PRT

<213> Mus musculus

<400> 38

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 10 15

Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly Tyr Met 20 25 30

His Trp Tyr Gln Gln Lys. Pro Gly Lys Ala Pro Lys Leu Trp Ile Tyr 35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp

Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr $85 \hspace{0.5cm} 90 \hspace{0.5cm} 95 \hspace{0.5cm}$

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105

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PCT/US02/32263

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Phe Gly Glu Thr Lys Met Ser Asn Ala Thr Leu Val Ser Tyr Ile Val

Gln Ile Leu Ser Arg Tyr Asp Ile Ala Leu Val Gln Glu Val Arg Asp

Ser His Leu Thr Ala Val Gly Lys Leu Leu Asp Asn Leu Asn Gln Asp

Ala Pro Asp Thr Tyr His Tyr Val Val Ser Glu Pro Leu Gly Arg Asn

Ser Tyr Lys Glu Arg Tyr Leu Phe Val Tyr Arg Pro Asp Gln Val Ser

Ala Val Asp Ser Tyr Tyr Tyr Asp Asp Gly Cys Glu Pro Cys Gly Asn

Asp Thr Phe Asn Arg Glu Pro Ala Ile Val Arg Phe Phe Ser Arg Phe

Thr Glu Val Arg Glu Phe Ala Ile Val Pro Leu His Ala Ala Pro Gly

Asp Ala Val Ala Glu Ile Asp Ala Leu Tyr Asp Val Tyr Leu Asp Val

Gln Glu Lys Trp Gly Leu Glu Asp Val Met Leu Met Gly Asp Phe Asn

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Trp Thr Ser Pro Thr Phe Gln Trp Leu Ile Pro Asp Ser Ala Asp Thr

Thr Ala Thr Pro Thr His Cys Ala Tyr Asp Arg Ile Val Val Ala Gly

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Lys Tyr Ala Ser Glu Ser Met Ser Gly Ile Pro Ser Arg Phe Ser Gly . 50

Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Thr Val Glu Ser 65 70 75 80

Glu Asp Ile Ala Asp Tyr Tyr Cys Gln Gln Ser His Ser Trp Pro Phe 85 90 95

Thr Phe Gly Ser Gly Thr Asn Leu Glu Val Lys Glu Val Lys Leu Glu

Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Met Lys Leu Ser 115 120 125

Cys Val Ala Ser Gly Phe Ile Phe Ser Asn His Trp Met Asn Trp Val 130 135 140

Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val Ala Glu Ile Arg Ser 145 150 155 160

Lys Ser Ile Asn Ser Ala Thr His Tyr Ala Glu Ser Val Lys Gly Arg 165 170 175

Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ala Val Tyr Leu Gln Met $180 \hspace{1cm} 185 \hspace{1cm} 185 \hspace{1cm} 190 \hspace{1cm}$

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Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly 50 60
Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu 65 70 75 80
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<210> 46 <211> 400 <212> PRT

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Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro 225 230 235 240

Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly

215

210

220

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Asp	Tyr	Gln 275	Gly	Met	Leu	Pro	Val 280	Cys	Pro	Leu	Leu	Pro 285	Gly	Thr	Ser		
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Thr 305	Ser	Met	Phe	Pro	Ser 310	Cys	Cys	Cys	Thr	Lys 315	Pro	Ser	Asp	Gly	Asn 320		
Cys	Thr	Cys	Ile	Pro 325	Ile	Pro	Ser	Ser	Trp 330	Ala	Phe	Ala	Arg	Phe 335	Leu		
Trp	Glu	Trp	Ala 340	Ser	Val	Arg	Phe	Ser 345	Trp	Leu	Ser	Leu	Leu 350	Val	Pro		
Phe	Val	Gln 355		Phe	Ala	Gly	Leu 360	Ser	Pro	Thr	Val	Trp 365	Leu	Ser	Val		
Ile	Trp 370		Met	Trp	Tyr	Trp 375	Gly	Pro	Ser	Leu	1 Tyr 380	Asn	Ile	Leu	Ser		
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-															gtetgea	180)
															aacagaa	240)
															cgacacc	300)

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Leu	Glu	Pro	Val	Gln	Phe	Leu	Arg	Ser	Val	Phe	Ala	Asn	Ser	Leu	Val

Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp Leu Leu Lys Asp Leu Glu 130 135 140

Glu Gly Ile Gln Thr Leu Met Gly Arg Leu Glu Asp Gly Ser Pro Arg 145 150 155 160

Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser Lys Phe Asp Thr Asn Ser 165 170 175

His Asn Asp Asp Ala Leu Leu Lys Asn Tyr Gly Leu Leu Tyr Cys Phe 180 189

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66/86

165 170 175

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr $_{180}$ $_{180}$ $_{185}$ $_{185}$

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr 195 200 205

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu 210 215 220

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys 225 230 235

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser 245 250 255

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp 260 265 270

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser 275 280 285

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<213> Homo sapiens

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Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr 202525

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$

Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro

Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp $85 \hspace{0.5cm} 90 \hspace{0.5cm} 95$

Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys

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Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 50 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln 65 70 75 80

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Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe 50 60

Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr 65 70 75 80

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Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe 50 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Thr Ala Tyr 65 70 75 80

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Tyr Tyr Thr Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75

Asp Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Val Lys Arg Thr Val Ala Ala 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 115 120 125

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Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205

Phe Asn Arg Gly Glu Cys 210

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<211> 448

<212> PRT

<213> Homo sapiens

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Gly Val Ile Tyr Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe

Lys Gly Arg Val Thr Leu Thr Val Asp Glu Ser Thr Asn Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys 85 90 95

Ala Arg Arg Asp Gly Asn Tyr Gly Trp Phe Ala Tyr Trp Gly Gln Gly 100 105 110

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe 115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu 130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Try 145 150 150

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu 165 170 175

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Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro 195 200

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Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp 260 265

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Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val 290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu 305 310 315

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys \$325\$ \$330\$

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr

350

345

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr

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